utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc if known. Please attach a copy of the cover sheet, pertinent claims, and abstract

Title of Invention: Borrelidin-producing polyketide synthase & the use

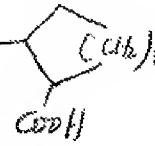
Inventors (please provide full names): Salas J A et al.

Earliest Priority Filing Date: 12/27/2002

For Sequence Searches Only Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

please search formula I and foramula 2 in claim 75 (see attached)

(a) In formula I

R_1 =  $n = 1, 2$

$R_5, R_{10} = OH$

$R_4 = CH_3, COOH, CN$

other R_8 - leave open

(b) in formula 2

$R_4, R_{10} = OH$

$R_4 = CH_3, COOH, CN$

other R - leave open

***** INVENTOR RESULTS *****

```
=> d his l42

     (FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 09:00:06 ON 04 SEP 2008)
               SAVE TEMP L41 KAM240MULTIN/A

     FILE 'HCAPLUS' ENTERED AT 09:04:34 ON 04 SEP 2008
L42            7 S ((L22-L31) AND L10) OR (L1 AND L10)

=> d que l42
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L2               SCR 2043 OR 1918
L3               STR
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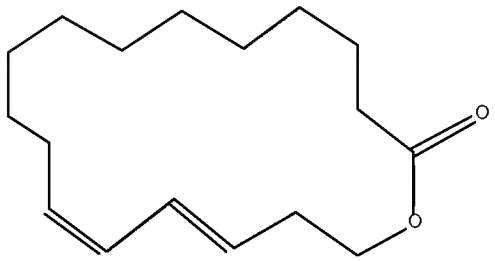

Structure attributes must be viewed using STN Express query preparation:

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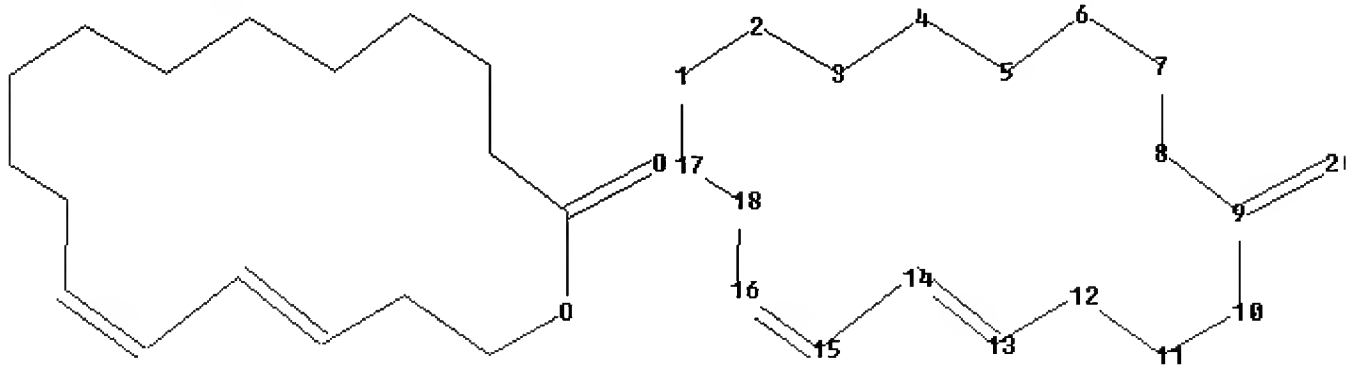
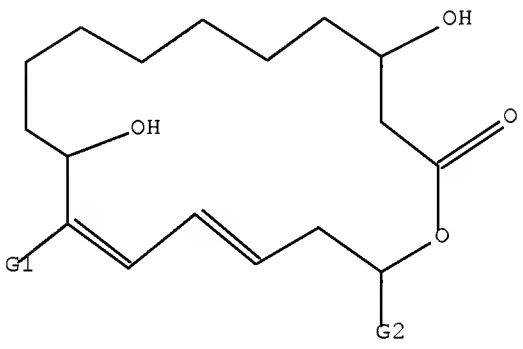


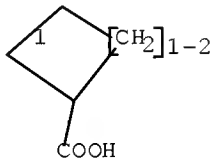

```
chain nodes :
20
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  17  18
chain bonds :
9-20
ring bonds :
1-2  1-17  2-3  3-4  4-5  5-6  6-7  7-8  8-9  9-10  10-11  11-12  12-13  13-14  14-
15
15-16  16-18  17-18
exact/norm bonds :
9-20
exact bonds :
1-2  1-17  2-3  3-4  4-5  5-6  6-7  7-8  8-9  9-10  10-11  11-12  12-13  13-14  14-
```

15
15-16 16-18 17-18
isolated ring systems :
containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 20:CLASS

L5 68 SEA FILE=REGISTRY SSS FUL L3 NOT L2
L6 STR





G1 Me,COOH,CN
G2 [@1],[@2],[@3]

Structure attributes must be viewed using STN Express query preparation:

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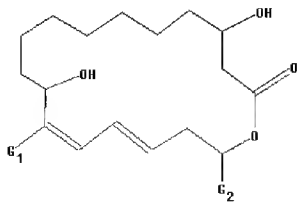

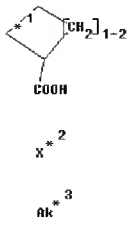

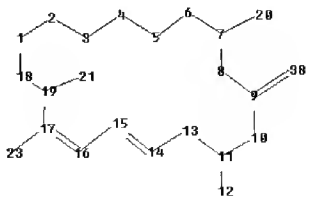

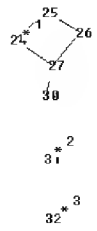

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12 20 21 23 30 31 32 38
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 13 14 15 16 17 18 19 24 25 26 27
chain bonds :
7-20 9-38 11-12 17-23 19-21 27-30
ring bonds :

```
1-2  1-18  2-3  3-4  4-5  5-6  6-7  7-8  8-9  9-10  10-11  11-13  13-14  14-15  15-
16
16-17  17-19  18-19  24-25  24-27  25-26  26-27
exact/norm bonds :
7-20  9-38  11-12  17-23  19-21
exact bonds :
1-2  1-18  2-3  3-4  4-5  5-6  6-7  7-8  8-9  9-10  10-11  11-13  13-14  14-15  15-
16
16-17  17-19  18-19  24-25  24-27  25-26  26-27  27-30
isolated ring systems :
containing 1 : 24 :


G1:CH3,COOH,CN

G2:[*1],[*2],[*3]

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:CLASS  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:Atom
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23:CLASS  24:Atom  25:Atom  26:Atom  27:Atom  30:CLASS  31:CLASS  32:CLASS
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L9            17 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L10           86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9
L22          478 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SALAS J?/AU
L23          305 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MENDEZ C?/AU
L24           51 SEA FILE=HCAPLUS ABB=ON  PLU=ON  OLANO C?/AU
L25         3325 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SANCHEZ C?/AU
L26          100 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BRANA A?/AU
L27          449 SEA FILE=HCAPLUS ABB=ON  PLU=ON  WILKINSON B?/AU
L28         5002 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MARTIN C?/AU
L29         1074 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MOSS S?/AU
L30          197 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LEADLAY P?/AU
L31           16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  OLIYNYK M?/AU
L42            7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (((L22 OR L23 OR L24 OR L25
                  OR L26 OR L27 OR L28 OR L29 OR L30 OR L31)) AND L10) OR (L1
                  AND L10)


=> d his l41

     (FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 09:00:06 ON 04 SEP 2008)
L41            6 S L40 AND BORRELIDIN

=> d que l41
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L23          305 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MENDEZ C?/AU
L24           51 SEA FILE=HCAPLUS ABB=ON  PLU=ON  OLANO C?/AU
L25         3325 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SANCHEZ C?/AU
L26          100 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BRANA A?/AU
L27          449 SEA FILE=HCAPLUS ABB=ON  PLU=ON  WILKINSON B?/AU
L28         5002 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MARTIN C?/AU
L29         1074 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MOSS S?/AU
L30          197 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LEADLAY P?/AU
L31           16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  OLIYNYK M?/AU
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L40 176 SEA ((L22 OR L23 OR L24 OR L25 OR L26 OR L27 OR L28 OR L29 OR L30 OR L31)) AND BIOSYNTHET? GENE#
L41 6 SEA L40 AND BORRELIDIN

=> dup rem l42 l41
FILE 'HCAPLUS' ENTERED AT 09:10:22 ON 04 SEP 2008
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PROCESSING COMPLETED FOR L42
PROCESSING COMPLETED FOR L41
L44 8 DUP REM L42 L41 (5 DUPLICATES REMOVED)
ANSWERS '1-7' FROM FILE HCAPLUS
ANSWER '8' FROM FILE BIOSIS

=> d l44 1-7 ibib abs hitstr; d l44 8 ibib ab

L44 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2004:547408 HCAPLUS Full-text
DOCUMENT NUMBER: 141:202986
TITLE: Biosynthesis of the angiogenesis inhibitor borrelidin by Streptomyces parvulus Tue4055: Insights into nitrile formation
AUTHOR(S): Olano, Carlos; Moss, Steven J.; Brana, Alfredo F.; Sheridan, Rose M.; Math, Vidya; Weston, Alison J.; Mendez, Carmen; Leadlay, Peter F.; Wilkinson, Barrie ; Salas, Jose A.
CORPORATE SOURCE: Departamento de Biologia Funcional e Instituto Universitario de Oncologia del Principado de Asturias (IUOPA), Universidad de Oviedo, Oviedo, 33006, Spain
SOURCE: Molecular Microbiology (2004), 52(6), 1745-1756
CODEN: MOMIEE; ISSN: 0950-382X
PUBLISHER: Blackwell Publishing Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The 18-membered polyketide macrolide borrelidin exhibits a number of important biol. activities, including potent angiogenesis inhibition. This has prompted two recent total syntheses as well as the cloning of the biosynthetic gene cluster from Streptomyces parvulus Tue4055. Borrelidin possesses some unusual structural characteristics, including a cyclopentane carboxylic acid moiety at C17 and a nitrile moiety at C12 of the macrocyclic ring. Nitrile groups are relatively rare in nature, and little is known of their biosynthesis during secondary metabolism The nitrile group of borrelidin is shown here to arise from the Me group of a methylmalonyl-CoA extender unit incorporated during polyketide chain extension. Insertional inactivation of two genes in the borrelidin gene cluster, borI (coding for a cytochrome P 450 monooxygenase) and borJ (coding for an aminotransferase), generated borrelidin non-producing mutants. These mutants accumulated different compds. lacking the C12 nitrile moiety, with the product of the borI-minus mutant (12-desnitrile-12-methyl-borrelidin) possessing a Me group and that of the borJ-minus mutant (12-

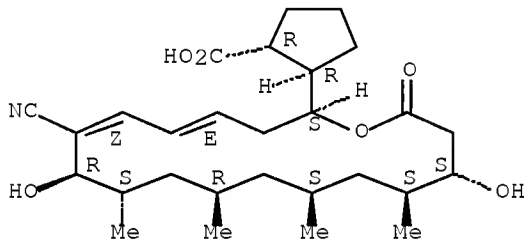
desnitrile-12-carboxyl-borrelidin) a carboxyl group at C12. The former but not the latter was converted into borrelidin when biotransformed by an S. parvulus mutant that is deficient in the biosynthesis of the borrelidin starter unit. This suggests that 12-desnitrile-12-methyl-borrelidin is a competent biosynthetic intermediate, whereas the carboxylated derivative is a shunt metabolite. Bioconversion of 12-desnitrile-12-methyl-borrelidin into borrelidin was also achieved in a heterologous system co-expressing borI and borJ in Streptomyces albus J1074. This bioconversion was more efficient when borK, which is believed to encode a dehydrogenase, was simultaneously expressed with borI and borJ. On the basis of these findings, a pathway is proposed for the formation of the nitrile moiety during borrelidin biosynthesis.

IT 7184-60-3, Borrelidin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(biosynthesis of angiogenesis inhibitor borrelidin by Streptomyces parvulus Tue4055 and formation of nitrile moiety)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 59 THERE ARE 59 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2004:96852 HCAPLUS Full-text
DOCUMENT NUMBER: 141:48175
TITLE: Biosynthesis of the Angiogenesis Inhibitor Borrelidin by Streptomyces parvulus Tu4055. Cluster Analysis and Assignment of Functions
AUTHOR(S): Olano, Carlos; Wilkinson, Barrie; Sanchez, Cesar; Moss, Steven J.; Sheridan, Rose; Math, Vidya; Weston, Alison J.; Brana, Alfredo F.; Martin, Christine J.; Oliynyk, Markiyan; Mendez, Carmen; Leadlay, Peter F.; Salas, Jose A.
CORPORATE SOURCE: Departamento de Biologia Funcional e Instituto Universitario de Oncologia del Principado de Asturias, Universidad de Oviedo, Oviedo, 33006, Spain
SOURCE: Chemistry & Biology (2004), 11(1), 87-97
CODEN: CBOLE2; ISSN: 1074-5521
PUBLISHER: Cell Press
DOCUMENT TYPE: Journal

LANGUAGE: English

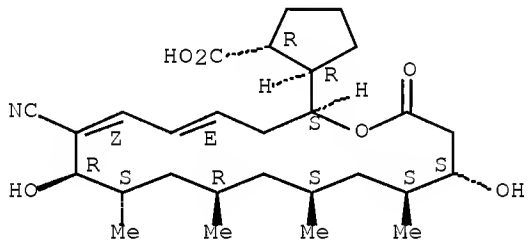
AB The biosynthetic gene cluster for the angiogenesis inhibitor borrelidin has been cloned from Streptomyces parvulus Tu4055. Sequence anal. indicates that the macrolide ring of borrelidin is formed by a modular polyketide synthase (PKS) (borA1-A6), a result that was confirmed by disruption of borA3. The borrelidin PKS is striking because only seven rather than the nine modules expected for a nonaketide product are encoded by borA1-A6. The starter unit of the PKS has been verified as trans-cyclopentane-1,2-dicarboxylic acid (trans-1,2-CPDA), and the genes involved in its biosynthesis identified. Other genes responsible for biosynthesis of the nitrile moiety, regulation, and self-resistance were also identified.

IT 7184-60-3, Borrelidin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sequence of borrelidin biosynthetic gene cluster of Streptomyces parvulus Tu4055)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:1364394 HCAPLUS Full-text
DOCUMENT NUMBER: 148:11000
TITLE: Preparation of borrelidin derivatives as anticancer agents
INVENTOR(S): Wilkinson, Barrie; Moss, Steven; Zhang, Ming
PATENT ASSIGNEE(S): Biotica Technology Limited, UK
SOURCE: PCT Int. Appl., 48pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2007135078	A2	20071129	WO 2007-EP54801	20070517
WO 2007135078	A3	20080221		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB,

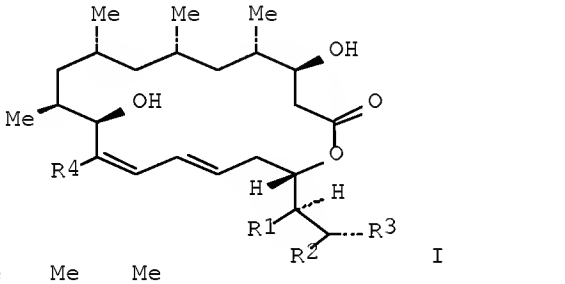
GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW

RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AP, EA, EP, OA

PRIORITY APPLN. INFO.: GB 2006-9981 A 20060519

OTHER SOURCE(S): CASREACT 148:11000; MARPAT 148:11000

GI



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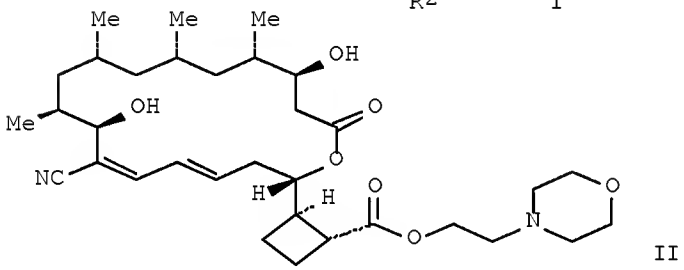


II

AB Borrelidin derivs. of formula I [R1, R2 = H, alkyl, etc.; R1R2 = CH2CH2, etc.; R3 = CONHR5, CO2R5, etc.; R4 = CN, CO2H, Me, CONH2; R5 = H, (substituted) alkyl, etc.] are prepared for the treatment of cancer or B-cell malignancies, or other diseases in which angiogenesis contributes to the pathol., including ophthalmic disorders such as diabetic retinopathy as well as age related macular degeneration (AMD), corneal neovascularization and retinopathy or prematurity. The present invention also provides methods for the production of these compds. and their use in medicine, in particular in the treatment and/or prophylaxis of cancer or B-cell malignancies and other diseases in which angiogenesis is implicated in the pathogenic process. Thus, II is prepared, and had 0.84 ratio of inhibition of CAM vasculature at 25 ng/CAM to in vitro cancer cell inhibition at 1 μM.

IT 724426-07-7P

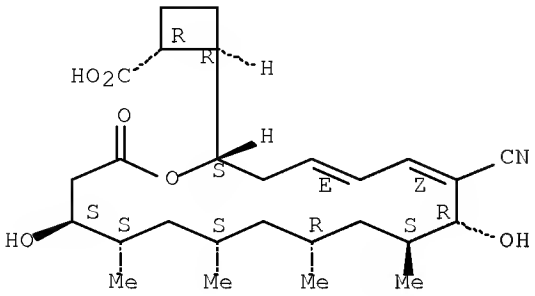
RL: PAC (Pharmacological activity); PUR (Purification or recovery); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)
(preparation of borrelidin derivs. as anticancer agents)

RN 724426-07-7 HCAPLUS

CN Cyclobutanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-

yl]-, (1R,2R)- (CA INDEX NAME)

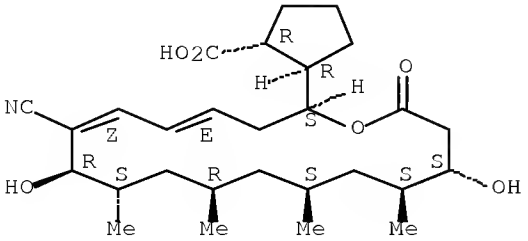
Absolute stereochemistry.
Double bond geometry as shown.



L44 ANSWER 4 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1048524 HCAPLUS Full-text
DOCUMENT NUMBER: 146:38421
TITLE: Separation of anti-angiogenic and cytotoxic activities of borrelidin by modification at the C17 side chain
AUTHOR(S): Wilkinson, Barrie; Gregory, Matthew A.; Moss, Steven J.; Carletti, Isabelle; Sheridan, Rose M.; Kaja, Andrew; Ward, Michael; Olano, Carlos; Mendez, Carmen; Salas, Jose A.; Leadlay, Peter F.; van Ginckel, Rob; Zhang, Ming-Qiang
CORPORATE SOURCE: Biotica Technology Ltd., Little Chesterford, Essex, CB10 1XL, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(22), 5814-5817
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A set of novel borrelidin analogs have been prepared by precursor-directed biosynthesis. Structure-activity relationship anal. suggests that steric structural arrangement within the C17 side chain is important for differentiating cytotoxic and antiangiogenic activities. A C17-cyclobutyl analog 3 was found to have markedly increased selectivity for in vitro angiogenesis inhibition over cytotoxicity and is therefore potentially useful as an anticancer agent.
IT 7184-60-3, Borrelidin 724426-05-5 724426-07-7 901327-48-8 901327-52-4 901327-55-7 901327-63-7
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(separation of anti-angiogenic and cytotoxic activities of borrelidin by modification at the C17 side chain)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

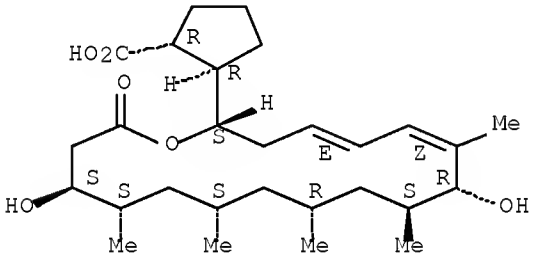
Absolute stereochemistry.

Double bond geometry as shown.



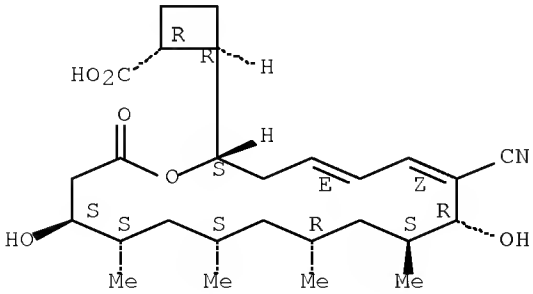
RN 724426-05-5 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-8,16-dihydroxy-7,9,11,13,15-pentamethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 724426-07-7 HCAPLUS
CN Cyclobutanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

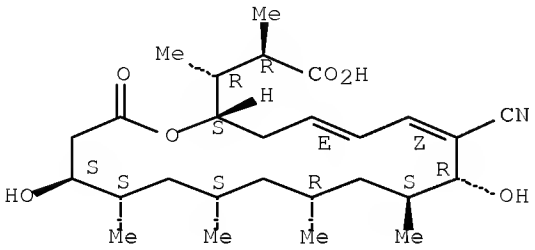
Absolute stereochemistry.
Double bond geometry as shown.



RN 901327-48-8 HCAPLUS

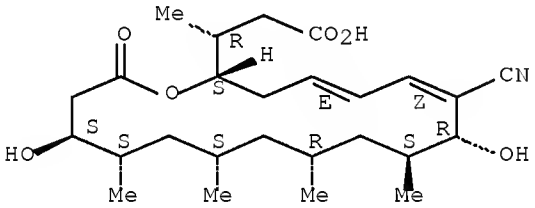
CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy-α,β,9,11,13,15-hexamethyl-18-oxo-, (αR,βR,2S,4E,6Z,8R,9S,11R,13S,15S,16S)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



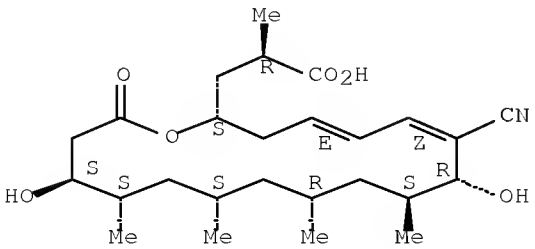
RN 901327-52-4 HCAPLUS
CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy-β,9,11,13,15-pentamethyl-18-oxo-, (βR,2S,4E,6Z,8R,9S,11R,13S,15S,16S)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



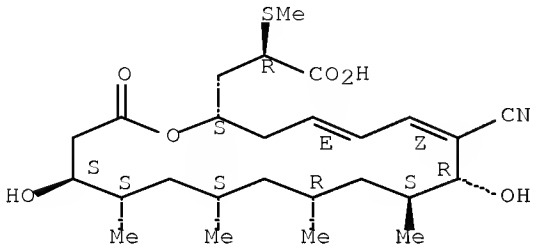
RN 901327-55-7 HCAPLUS
CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy-α,9,11,13,15-pentamethyl-18-oxo-, (αR,2S,4E,6Z,8R,9S,11R,13S,15S,16S)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 901327-63-7 HCAPLUS
CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-α-(methylthio)-18-oxo-, (αR,2S,4E,6Z,8R,9S,11R,13S,15S,16S)- (CA INDEX NAME)

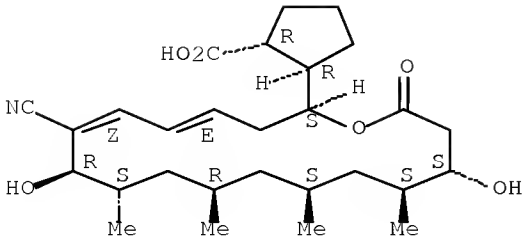
Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 5 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:507221 HCAPLUS Full-text
DOCUMENT NUMBER: 145:165577
TITLE: Biosynthesis of the angiogenesis inhibitor borrelidin: directed biosynthesis of novel analogues
AUTHOR(S): Moss, Steven J.; Carletti, Isabelle; Olano, Carlos; Sheridan, Rose M.; Ward, Michael; Math, Vidya; Nur-E-Alam, Mohammad; Brana, Alfredo F.; Zhang, Ming Qiang; Leadlay, Peter F.; Mendez, Carmen; Salas, Jose A.; Wilkinson, Barrie
CORPORATE SOURCE: Biotica, Little Chesterford, CB10 1XL, UK
SOURCE: Chemical Communications (Cambridge, United Kingdom) (2006), (22), 2341-2343
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:165577
AB We report the directed biosynthesis of borrelidin analogs and their selective anti-proliferative activity against human cancer cell lines.
IT 7184-60-3P, Borrelidin
RL: BMF (Bioindustrial manufacture); BIOL (Biological study); PREP (Preparation)
(directed biosynthesis of novel borrelidin analogs)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

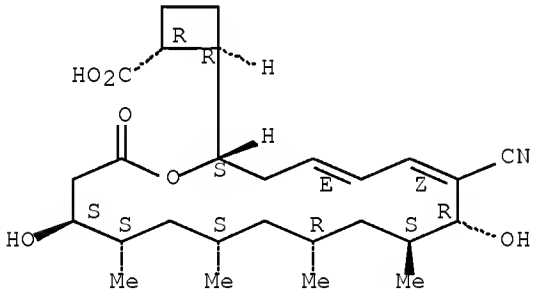


IT 724426-07-7P 901327-46-8P 901327-52-4P
901327-55-7P 901327-59-1P 901327-63-7P
RL: BMF (Bioindustrial manufacture); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
(directed biosynthesis of novel borrelidin analogs)

RN 724426-07-7 HCAPLUS

CN Cyclobutanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

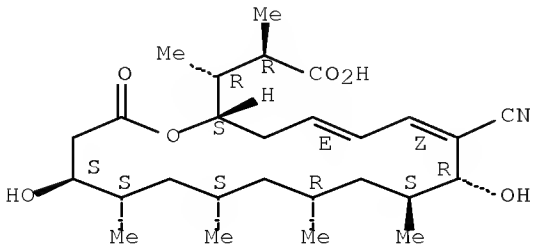
Absolute stereochemistry.
Double bond geometry as shown.



RN 901327-48-8 HCAPLUS

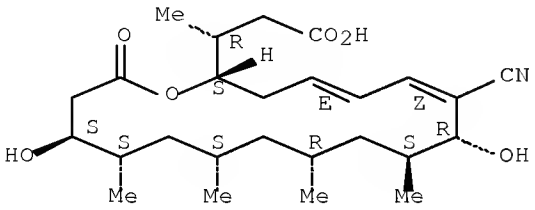
CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy-α,β,9,11,13,15-hexamethyl-18-oxo-, (αR,βR,2S,4E,6Z,8R,9S,11R,13S,15S,16S)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



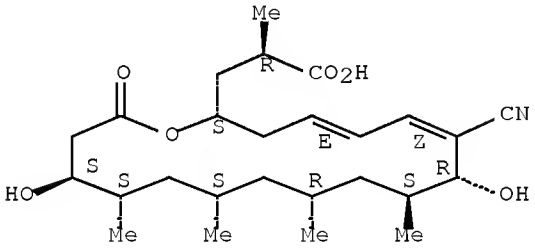
RN 901327-52-4 HCAPLUS
CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy-β,9,11,13,15-pentamethyl-18-oxo-, (βR,2S,4E,6Z,8R,9S,11R,13S,15S,16S)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



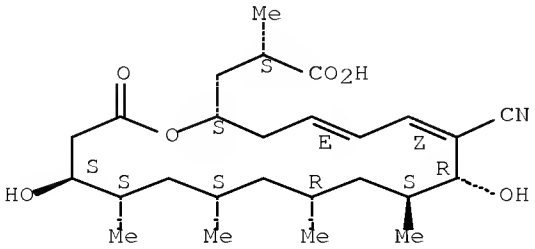
RN 901327-55-7 HCAPLUS
CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy-α,9,11,13,15-pentamethyl-18-oxo-, (αR,2S,4E,6Z,8R,9S,11R,13S,15S,16S)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



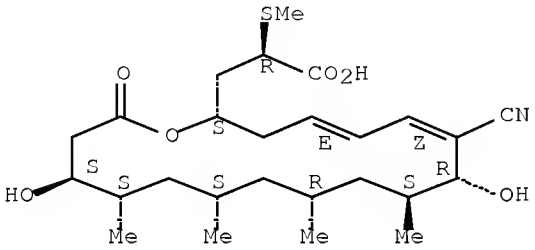
RN 901327-59-1 HCAPLUS
CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy-α,9,11,13,15-pentamethyl-18-oxo-, (αS,2S,4E,6Z,8R,9S,11R,13S,15S,16S)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 901327-63-7 HCAPLUS
CN Oxacyclooctadeca-4,6-diene-2-propanoic acid, 7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-α-(methylthio)-18-oxo-, (αR,2S,4E,6Z,8R,9S,11R,13S,15S,16S)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:570032 HCAPLUS Full-text
DOCUMENT NUMBER: 141:118341
TITLE: The borrelidin biosynthetic gene cluster of Streptomyces parvulus Tu4055 and its use in the development of novel polyketide with therapeutic uses
INVENTOR(S): Salas, Jose A.; Mendez, Carmen; Olano, Carlos; Sanchez, Cesar; Brana, Alfredo F.; Wilkinson, Barrie ; Martin, Christine J.; Moss, Steven ; Leadlay, Peter F.; Oliynyk, Marko
PATENT ASSIGNEE(S): Biotica Technology Limited, UK; The University of Oviedo
SOURCE: PCT Int. Appl., 255 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004058976	A2	20040715	WO 2003-GB5704	20031224
WO 2004058976	A3	20050217		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

CA 2506669	A1	20040715	CA 2003-2506669		20031224
AU 2003295169	A1	20040722	AU 2003-295169		20031224
EP 1576160	A2	20050921	EP 2003-786170		20031224
EP 1576160	B1	20070502			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK					
BR 2003017118	A	20051025	BR 2003-17118		20031224
CN 1732264	A	20060208	CN 2003-80107717		20031224
JP 2006514548	T	20060511	JP 2004-563382		20031224
AT 361286	T	20070515	AT 2003-786170		20031224
EP 1840216	A2	20071003	EP 2007-107182		20031224
EP 1840216	A3	20071017			
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ES 2287552	T3	20071216	ES 2003-786170		20031224
EP 1961747	A2	20080827	EP 2007-106112		20031224
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IN 2005KN00733	A	20060324	IN 2005-KN733		20050426
MX 2005PA05323	A	20060310	MX 2005-PA5323		20050518
US 20070065920	A1	20070322	US 2006-534210		20060317 <--
IN 2007KN01744	A	20080801	IN 2007-KN1744		20070516
IN 2007KN01745	A	20080801	IN 2007-KN1745		20070516
PRIORITY APPLN. INFO.:			GB 2002-30217	A	20021227
			EP 2003-786170	A3	20031224
			WO 2003-GB5704	W	20031224
			IN 2005-KN733	A3	20050426

OTHER SOURCE(S): MARPAT 141:118341

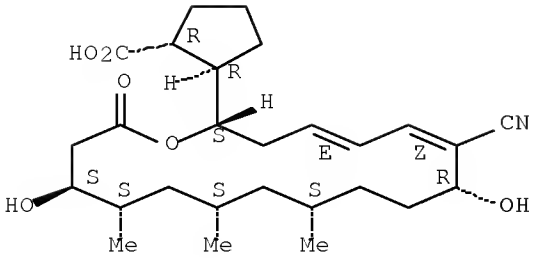
AB The biosynthetic gene cluster for the angiogenesis inhibitor borrelidin of Streptomyces parvulus Tu4055 is cloned and characterized. The coding regions for the individual domains of the enzyme may be used in the development of novel polyketide synthases for the manufacture of novel polyketides including borrelidin and analogs and derivs. The macrolide ring of borrelidin is formed by a modular polyketide synthase (PKS) encoded by six open reading frames (borA1-A6), a result that was confirmed by disruption of the borA3 open reading frame. The borrelidin PKS is striking because only seven rather than the nine modules expected for a nonaketide product are encoded by borA1-A6. The starter unit of the PKS has been verified as trans-cyclopentane-1,2-dicarboxylic acid (trans-1,2-CPDA), and the genes involved in its biosynthesis identified. Cloning of the genes by expression in Escherichia coli is described. Other genes responsible for biosynthesis of the nitrile moiety, regulation, and self-resistance are also identified.

IT 196869-69-9 724426-05-5 724426-06-6
724426-07-7
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(biosynthesis of, with engineered borrelidin synthase; borrelidin biosynthetic gene cluster of Streptomyces parvulus Tu4055 and its use in development of novel polyketide with therapeutic uses)

RN 196869-69-9 HCAPLUS

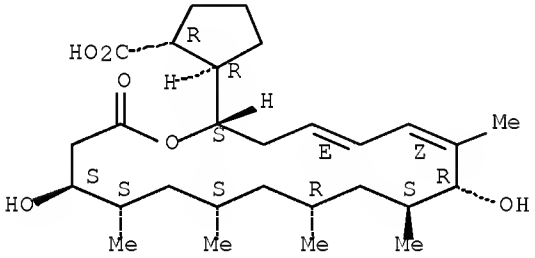
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,11S,13S,15S,16S)-7-cyano-8,16-dihydroxy-11,13,15-trimethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



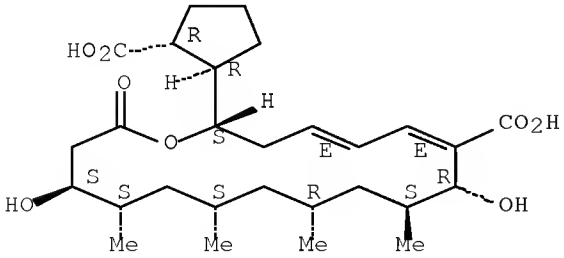
RN 724426-05-5 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-8,16-dihydroxy-7,9,11,13,15-pentamethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



RN 724426-06-6 HCAPLUS
CN Oxacyclooctadeca-4,6-diene-7-carboxylic acid, 2-[(1R,2R)-2-carboxycyclopentyl]-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxo-, (2S,4E,6E,8R,9S,11R,13S,15S,16S)- (CA INDEX NAME)

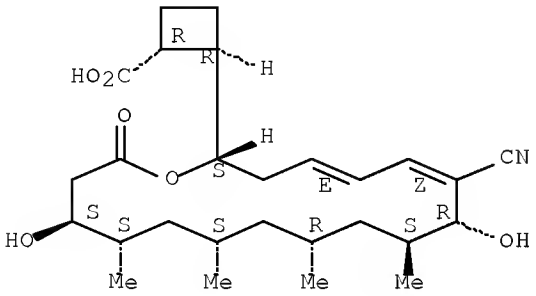
Absolute stereochemistry.
Double bond geometry as shown.



RN 724426-07-7 HCAPLUS
CN Cyclobutanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-

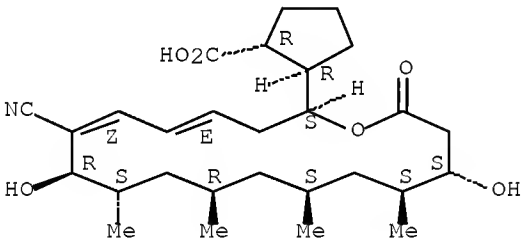
yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IT 7184-60-3P, Borrelidin
RL: BPN (Biosynthetic preparation); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation)
(gene cluster for biosynthesis of; borrelidin biosynthetic gene cluster of Streptomyces parvulus Tu4055 and its use in development of novel polyketide with therapeutic uses)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



L44 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2003:857652 HCAPLUS Full-text
DOCUMENT NUMBER: 140:195301
TITLE: Evidence from engineered gene fusions for the repeated use of a module in a modular polyketide synthase
AUTHOR(S): Olano, Carlos; Wilkinson, Barrie; Moss, Steven J.; Brana, Alfredo F.; Mendez, Carmen; Leadlay, Peter F.; Salas, Jose A.
CORPORATE SOURCE: Departamento de Biologia Funcional e Instituto Universitario de Oncologia del Principado de Asturias (I.U.O.P.A), Universidad de Oviedo, Oviedo, 33006, Spain

SOURCE: Chemical Communications (Cambridge, United Kingdom) (2003), (22), 2780-2782
CODEN: CHCOFS; ISSN: 1359-7345
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English

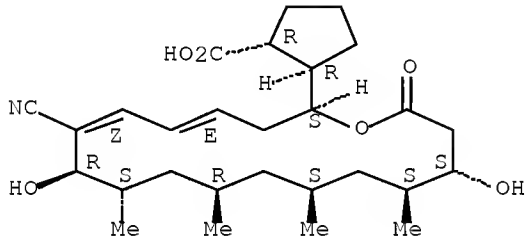
AB Functional evidence for programmed loss of co-linearity on the borrelidin modular polyketide synthase (PKS) is presented.

IT 7184-60-3, Borrelidin
RL: BSU (Biological study, unclassified); BIOL (Biological study) (evidence from engineered gene fusions for repeated use of a module in borrelidin modular polyketide synthase)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L44 ANSWER 8 OF 8 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:589076 BIOSIS Full-text
DOCUMENT NUMBER: PREV200600599702
TITLE: Potent angiogenesis inhibitors derived from borrelidin: SAR and antitumor activities.
AUTHOR(S): Wilkinson, Barrie [Reprint Author]; Moss, Steven J.; Carletti, Isabelle; Vousden, William; Coates, Nigel; Olano, Carlos; Sheridan, Rose M.; Mendez, Carmen; Salas, Jose A.; Leadlay, Peter F.; Zhang, Ming-Qiang
CORPORATE SOURCE: Univ Oviedo, Dept Biol Funct, Oviedo, Spain
SOURCE: Proceedings of the American Association for Cancer Research Annual Meeting, (APR 2006) Vol. 47, pp. 1344.
Meeting Info.: 97th Annual Meeting of the American-Association-for-Cancer-Research (AACR). Washington, DC, USA. April 01 -05, 2006. Amer Assoc Canc Res.
ISSN: 0197-016X.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 8 Nov 2006
Last Updated on STN: 8 Nov 2006

***** QUERY RESULTS *****

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L3               STR
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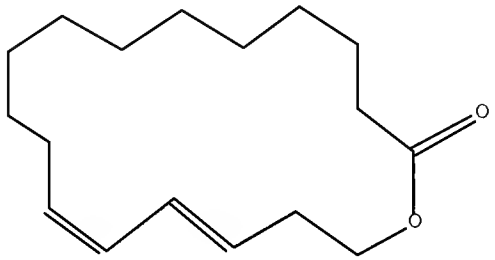

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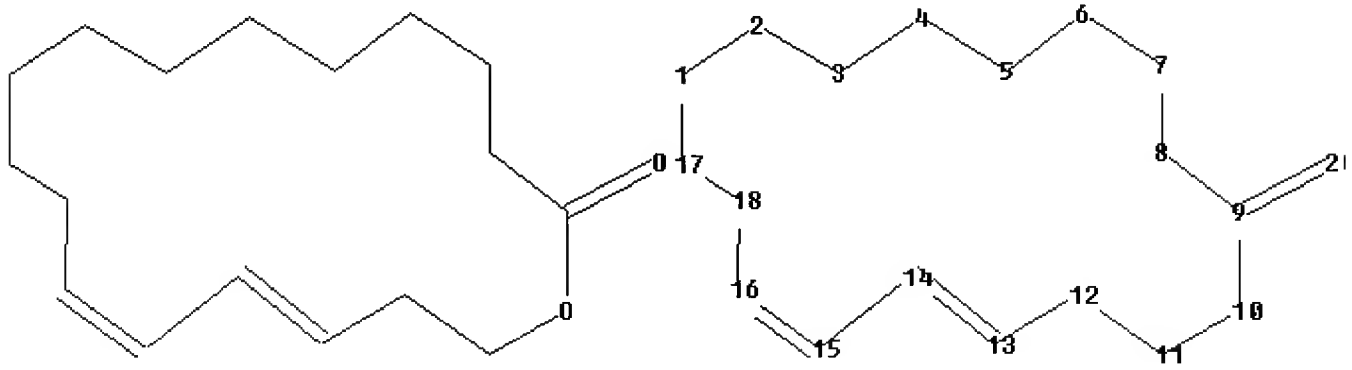
Uploading L11.str

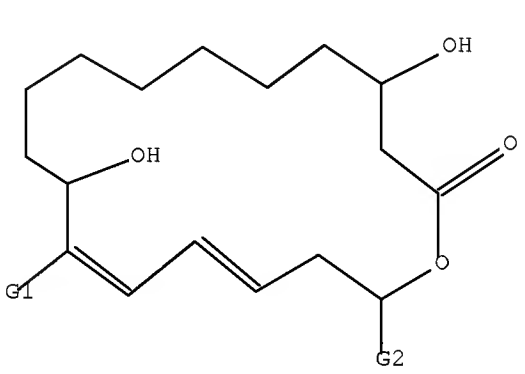


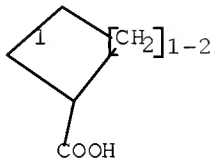

```
chain nodes :
20
ring nodes :
1  2  3  4  5  6  7  8  9  10  11  12  13  14  15  16  17  18
chain bonds :
9-20
ring bonds :
1-2  1-17  2-3  3-4  4-5  5-6  6-7  7-8  8-9  9-10  10-11  11-12  12-13  13-14  14-
15
15-16  16-18  17-18
exact/norm bonds :
9-20
exact bonds :
1-2  1-17  2-3  3-4  4-5  5-6  6-7  7-8  8-9  9-10  10-11  11-12  12-13  13-14  14-
15
15-16  16-18  17-18
isolated ring systems :
```

containing 1 :

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 20:CLASS

L5 68 SEA FILE=REGISTRY SSS FUL L3 NOT L2
L6 STR





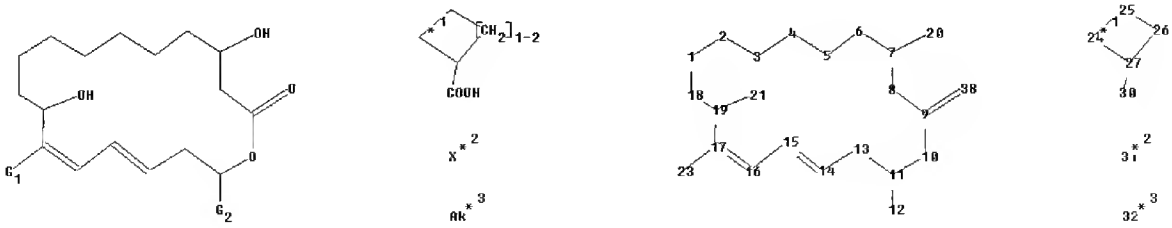
X 2

Ak 3

G1 Me,COOH,CN
G2 [@1],[@2],[@3]

Structure attributes must be viewed using STN Express query preparation:

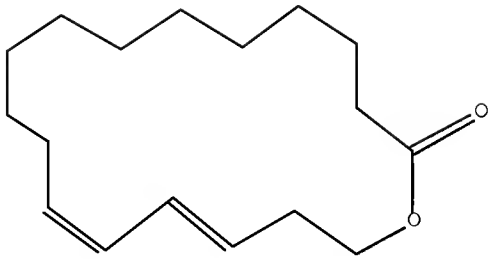
Uploading L12.str



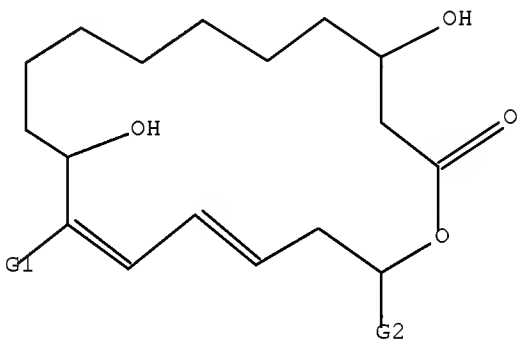
chain nodes :
12 20 21 23 30 31 32 38
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 13 14 15 16 17 18 19 24 25 26 27
chain bonds :
7-20 9-38 11-12 17-23 19-21 27-30
ring bonds :
1-2 1-18 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-13 13-14 14-15 15-16
16-17 17-19 18-19 24-25 24-27 25-26 26-27

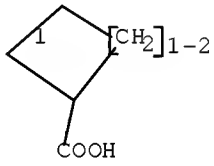
```
exact/norm bonds :
7-20  9-38  11-12  17-23  19-21
exact bonds :
1-2  1-18  2-3  3-4  4-5  5-6  6-7  7-8  8-9  9-10  10-11  11-13  13-14  14-15  15-
16
16-17  17-19  18-19  24-25  24-27  25-26  26-27  27-30
isolated ring systems :
containing 1 : 24 :


G1:CH3,COOH,CN

G2:[*1],[*2],[*3]

Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:CLASS  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  19:Atom
20:CLASS  21:CLASS
23:CLASS  24:Atom  25:Atom  26:Atom  27:Atom  30:CLASS  31:CLASS  32:CLASS
38:CLASS



L9            17 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L10           86 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L9
L11           14 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND 3/SC,SX
L12         5382 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BIOSYNTHE? GENE#
L13            4 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND L12
L14         5465 SEA FILE=HCAPLUS ABB=ON  PLU=ON  POLYKETID?
L15            6 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND L14
L16           18 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L11 OR L13 OR L15
L17           19 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND PHARMAC?/SC,SX
L18           33 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L16 OR L17
L19        36472 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BIOSYNTHET?
L20            9 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L10 AND L19
L21           37 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L18 OR L20
L22          478 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SALAS J?/AU
L23          305 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MENDEZ C?/AU
L24           51 SEA FILE=HCAPLUS ABB=ON  PLU=ON  OLANO C?/AU
L25         3325 SEA FILE=HCAPLUS ABB=ON  PLU=ON  SANCHEZ C?/AU
L26          100 SEA FILE=HCAPLUS ABB=ON  PLU=ON  BRANA A?/AU
L27          449 SEA FILE=HCAPLUS ABB=ON  PLU=ON  WILKINSON B?/AU
L28         5002 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MARTIN C?/AU
L29         1074 SEA FILE=HCAPLUS ABB=ON  PLU=ON  MOSS S?/AU
L30          197 SEA FILE=HCAPLUS ABB=ON  PLU=ON  LEADLAY P?/AU
L31           16 SEA FILE=HCAPLUS ABB=ON  PLU=ON  OLIYNYK M?/AU
L42            7 SEA FILE=HCAPLUS ABB=ON  PLU=ON  (((L22 OR L23 OR L24 OR L25
                  OR L26 OR L27 OR L28 OR L29 OR L30 OR L31)) AND L10) OR (L1
                  AND L10)
L43           30 SEA FILE=HCAPLUS ABB=ON  PLU=ON  L21 NOT L42


=> d his l34

     (FILE 'MEDLINE' ENTERED AT 08:57:41 ON 04 SEP 2008)
L34            3 S L33 AND BIOSYNTHET?

=> d que l34
L2               SCR 2043 OR 1918
```

L3 STR



Structure attributes must be viewed using STN Express query preparation.
L5 68 SEA FILE=REGISTRY SSS FUL L3 NOT L2
L6 STR





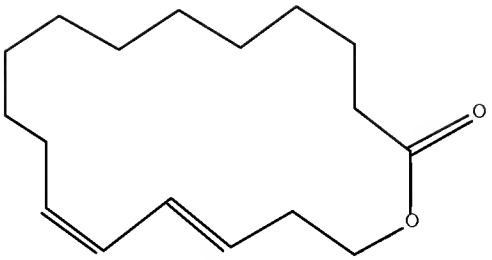
G1 Me,COOH,CN
G2 [@1],[@2],[@3]

Structure attributes must be viewed using STN Express query preparation.
L9 17 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L32 1 SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND (MEDLINE OR BIOSIS OR DRUGU OR EMBASE)/LC
L33 31 SEA FILE=MEDLINE ABB=ON PLU=ON L32
L34 3 SEA FILE=MEDLINE ABB=ON PLU=ON L33 AND BIOSYNTHET?

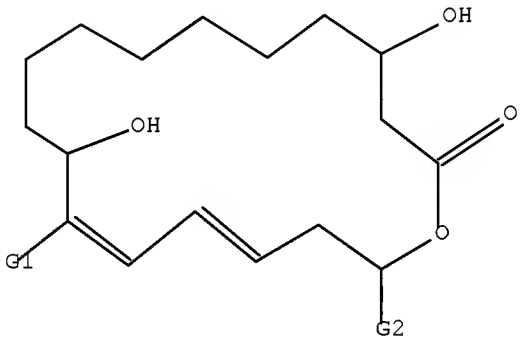
=> d his l36

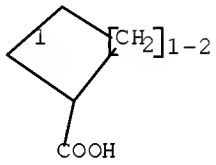
(FILE 'BIOSIS' ENTERED AT 08:58:27 ON 04 SEP 2008)
L36 6 S L33 AND BIOSYNTHET?

=> d que l36
L2 SCR 2043 OR 1918
L3 STR



Structure attributes must be viewed using STN Express query preparation.
L5 68 SEA FILE=REGISTRY SSS FUL L3 NOT L2
L6 STR





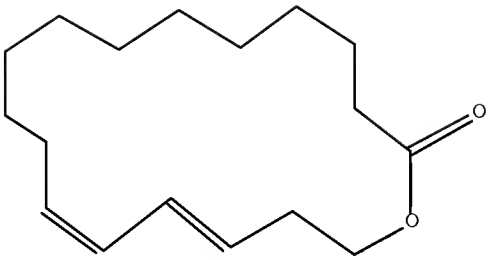
G1 Me,COOH,CN
G2 [@1],[@2],[@3]

Structure attributes must be viewed using STN Express query preparation.
L9 17 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L32 1 SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND (MEDLINE OR BIOSIS OR DRUGU OR EMBASE)/LC
L33 31 SEA FILE=MEDLINE ABB=ON PLU=ON L32
L36 6 SEA FILE=BIOSIS ABB=ON PLU=ON L33 AND BIOSYNTHET?

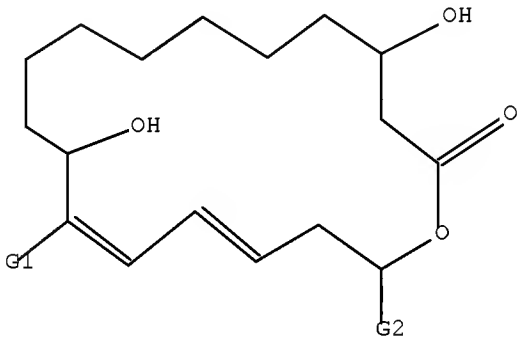
=> d his l38

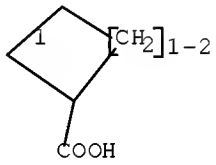
(FILE 'DRUGU' ENTERED AT 08:58:53 ON 04 SEP 2008)
L38 8 S L33

=> d que l38
L2 SCR 2043 OR 1918
L3 STR



Structure attributes must be viewed using STN Express query preparation.
L5 68 SEA FILE=REGISTRY SSS FUL L3 NOT L2
L6 STR





G1 Me,COOH,CN
G2 [@1],[@2],[@3]

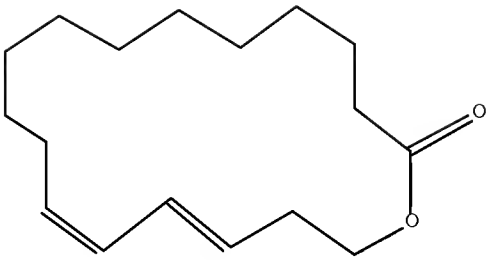
Structure attributes must be viewed using STN Express query preparation.
L9 17 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L32 1 SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND (MEDLINE OR BIOSIS OR DRUGU OR EMBASE)/LC
L38 8 SEA FILE=DRUGU ABB=ON PLU=ON L32

=> d his l39

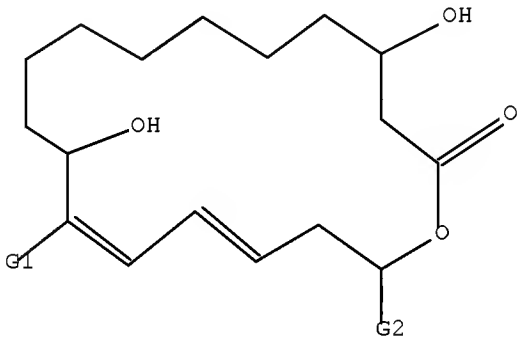
(FILE 'DRUGU' ENTERED AT 08:58:53 ON 04 SEP 2008)

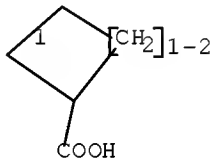
FILE 'EMBASE' ENTERED AT 08:59:36 ON 04 SEP 2008
L39 3 S L33 AND BIOSYNTHET?

=> d que l39
L2 SCR 2043 OR 1918
L3 STR



Structure attributes must be viewed using STN Express query preparation.
L5 68 SEA FILE=REGISTRY SSS FUL L3 NOT L2
L6 STR





G1 Me,COOH,CN
G2 [@1],[@2],[@3]

Structure attributes must be viewed using STN Express query preparation.
L9 17 SEA FILE=REGISTRY SUB=L5 SSS FUL L6
L32 1 SEA FILE=REGISTRY ABB=ON PLU=ON L9 AND (MEDLINE OR BIOSIS OR DRUGU OR EMBASE)/LC
L33 31 SEA FILE=MEDLINE ABB=ON PLU=ON L32
L39 3 SEA FILE=EMBASE ABB=ON PLU=ON L33 AND BIOSYNTHET?

=> dup rem l43 l34 l36 l38 l39
FILE 'HCAPLUS' ENTERED AT 09:11:54 ON 04 SEP 2008
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2008 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'MEDLINE' ENTERED AT 09:11:54 ON 04 SEP 2008

FILE 'BIOSIS' ENTERED AT 09:11:54 ON 04 SEP 2008
Copyright (c) 2008 The Thomson Corporation

FILE 'DRUGU' ENTERED AT 09:11:54 ON 04 SEP 2008

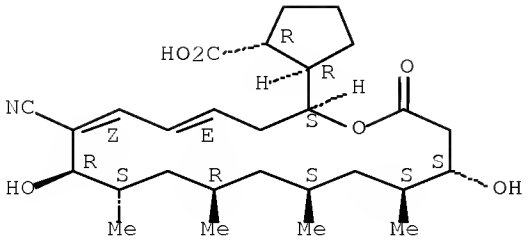
FILE 'EMBASE' ENTERED AT 09:11:54 ON 04 SEP 2008

PROCESSING COMPLETED FOR L43
PROCESSING COMPLETED FOR L34
PROCESSING COMPLETED FOR L36
PROCESSING COMPLETED FOR L38
PROCESSING COMPLETED FOR L39
L45 40 DUP REM L43 L34 L36 L38 L39 (10 DUPLICATES REMOVED)
ANSWERS '1-30' FROM FILE HCAPLUS
ANSWERS '31-32' FROM FILE MEDLINE
ANSWER '33' FROM FILE BIOSIS
ANSWERS '34-39' FROM FILE DRUGU
ANSWER '40' FROM FILE EMBASE

=> d l45 1-30 ibib abs fhitstr hitind; d l45 31-40 ibib ab hitind

L45 ANSWER 1 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 2003:442770 HCAPLUS Full-text
DOCUMENT NUMBER: 139:159699
TITLE: Borrelidin induces the transcription of amino acid biosynthetic enzymes via a GCN4-dependent pathway
AUTHOR(S): Eastwood, Erin L.; Schaus, Scott E.
CORPORATE SOURCE: Metcalf Center for Science and Engineering, Department of Chemistry, Boston University, Boston, MA, 02215, USA
SOURCE: Bioorganic & Medicinal Chemistry Letters (2003), 13(13), 2235-2237
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Global cellular profiling of mRNA levels has been used to provide insight into the effects of the angiogenesis inhibitor borrelidin on the eukaryotic model organism Saccharomyces cerevisiae. The most notable result of treatment with borrelidin is the induction of amino acid biosynthetic enzymes in a time-dependent fashion. We have ascertained that induction of this pathway involves the GCN4 transcription factor. This conclusion was determined by treating a yeast strain lacking this gene and observing the absence of increased gene transcription under Gcn4p control.
IT 7184-60-3, Borrelidin
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(borrelidin induces transcription of amino acid biosynthetic enzymes via a GCN4-dependent pathway)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 1-8 (Pharmacology)
ST amino acid biosynthetic enzyme borrelidin GCN4
IT Transcription factors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GCN4; borrelidin induces transcription of amino acid biosynthetic enzymes via a GCN4-dependent pathway)
IT Transcription, genetic
(borrelidin induces transcription of amino acid biosynthetic enzymes via a GCN4-dependent pathway)
IT Amino acids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(borrelidin induces transcription of amino acid biosynthetic enzymes via a GCN4-dependent pathway)
IT 7184-60-3, Borrelidin
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(borrelidin induces transcription of amino acid biosynthetic enzymes via a GCN4-dependent pathway)
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 2 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 2003:695485 HCAPLUS Full-text
DOCUMENT NUMBER: 140:70527
TITLE: Anti-angiogenesis effects of borrelidin are mediated through distinct pathways: Threonyl-tRNA synthetase and caspases are independently involved in suppression of proliferation and induction of apoptosis in endothelial cells
AUTHOR(S): Kawamura, Takanori; Liu, Diana; Towle, Murray J.; Kageyama, Rena; Tsukahara, Naoko; Wakabayashi, Toshiaki; Littlefield, Bruce A.
CORPORATE SOURCE: Eisai Research Institute, Andover, MA, 01810-2441, USA
SOURCE: Journal of Antibiotics (2003), 56(8), 709-715
CODEN: JANTAJ; ISSN: 0021-8820
PUBLISHER: Japan Antibiotics Research Association
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Borrelidin, an antibiotic with anti-angiogenic activity, not only suppresses new capillary tube formation, but also collapses formed capillary tubes in a rat aorta culture model. Since it selectively inhibits threonyl-tRNA synthetase, we examined the effect of threonine on its anti-angiogenic activity. We found that a high concentration of threonine (1 mM) attenuated the ability of borrelidin to inhibit both capillary tube formation in the rat aorta culture model and human umbilical vein endothelial cells (HUVEC) proliferation, yet did not affect the ability of borrelidin to collapse formed capillary tubes or to induce apoptosis in HUVEC. Borrelidin activated

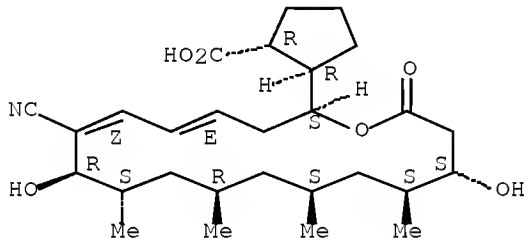
caspase-3 and -8, and inhibitors of both caspase-3 and -8 suppressed borrelidin-induced apoptosis in HUVEC. Taken together, these data suggest that the anti-angiogenic effects of borrelidin are mediated through at least two mechanisms, i.e. one threonine-dependent and the other threonine-independent, and borrelidin induces apoptosis in endothelial cells via the caspase-8/-3 pathway.

IT 7184-60-3, Borrelidin
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanisms of antiangiogenic effects of borrelidin)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 1-6 (Pharmacology)

IT 7184-60-3, Borrelidin
RL: DMA (Drug mechanism of action); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mechanisms of antiangiogenic effects of borrelidin)

REFERENCE COUNT: 16 THERE ARE 16 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 3 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 5

ACCESSION NUMBER: 1997:578984 HCAPLUS Full-text

DOCUMENT NUMBER: 127:242909

ORIGINAL REFERENCE NO.: 127:47239a,47242a

TITLE: Borrelidin is an angiogenesis inhibitor; disruption of angiogenic capillary vessels in a rat aorta matrix culture model

AUTHOR(S): Wakabayashi, Toshiaki; Kageyama, Rena; Naruse, Nobuaki; Tsukahara, Naoko; Funahashi, Yasuhiro; Kitoh, Kyosuke; Watanabe, Yoshio

CORPORATE SOURCE: Tsukuba Research Laboratories, Eisai, Co., Ltd., Tsukuba, 300-26, Japan

SOURCE: Journal of Antibiotics (1997), 50(8), 671-676
CODEN: JANTAJ; ISSN: 0021-8820

PUBLISHER: Japan Antibiotics Research Association

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Borrelidin, an antibiotic from Streptomyces rochei, was found to be an angiogenesis inhibitor in a rat aorta matrix culture model which forms capillary vessels in vitro. Borrelidin strongly inhibited capillary tube formation with a 50%-inhibitory concentration value of 0.8 nM, and decreased

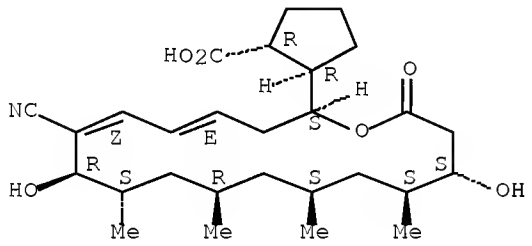
the number of capillary tubes within 24 h when added after maturation of tube formation. Borrelidin remarkably disrupted capillary tubes in a dose-dependent manner, by inducing apoptosis of the tube-forming cells.

IT 7184-60-3, Borrelidin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiogenesis inhibition by borrelidin)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 1-6 (Pharmacology)

IT 7184-60-3, Borrelidin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(angiogenesis inhibition by borrelidin)

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 4 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 6

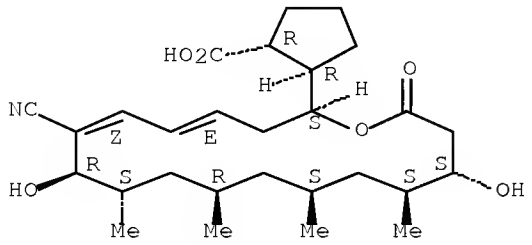
ACCESSION NUMBER: 1971:20712 HCAPLUS Full-text
DOCUMENT NUMBER: 74:20712
ORIGINAL REFERENCE NO.: 74:3331a,3334a
TITLE: Effect of borrelidin on the threonyl-tRNA-synthetase activity and the regulation of threonine-biosynthetic enzymes in Saccharomyces cerevisiae
AUTHOR(S): Nass, Gisela; Hasenbank, R.
CORPORATE SOURCE: Max-Planck-Inst. Mol. Genet., Berlin, Fed. Rep. Ger.
SOURCE: Molecular and General Genetics (1970), 108(1), 28-32
CODEN: MGGEAE; ISSN: 0026-8925
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Threonyl-tRNA (transfer RNA) synthetase and aspartokinase levels were depressed 20-and 2-fold, resp., when yeast cells were grown in the presence of 0.5 g/ml borrelidin. When threonine (0.37 mg/ml) or homo-serine (1.4 mg/ml) was included in the medium, borrelidin had no effect on aspartokinase level. Threonyl-tRNA synthetase may be involved in repression of formation of the threonine bio-synthetic enzyme.

IT 7184-60-3
RL: BIOL (Biological study)

(threonine-forming enzymes inhibition by, in Saccharomyces cerevisiae)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 8 (Microbial Biochemistry)
IT 7184-60-3
RL: BIOL (Biological study)
(threonine-forming enzymes inhibition by, in Saccharomyces cerevisiae)

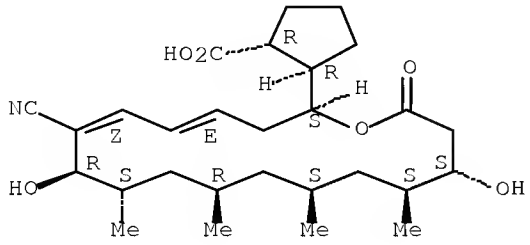
L45 ANSWER 5 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 1969:55138 HCAPLUS Full-text
DOCUMENT NUMBER: 70:55138
ORIGINAL REFERENCE NO.: 70:10353a,10356a
TITLE: Effect of the antibiotic, borrelidin, on the regulation of threonine biosynthetic enzymes in Escherichia coli
AUTHOR(S): Nass, Gisela; Poralla, K.; Zaehner, Hans
CORPORATE SOURCE: Max-Planck-Inst. Mol. Genet., Berlin, Fed. Rep. Ger.
SOURCE: Biochemical and Biophysical Research Communications (1969), 34(1), 84-91
CODEN: BBRCA9; ISSN: 0006-291X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Borrelidin (0.7 or 7.0 μg./ml.) almost abolished threonyl-tRNA synthetase activity in cell-free exts. of E. coli K12 or E. coli B; it did not affect methionyl-tRNA, arginyl-tRNA, phenylalanyl-tRNA, isoleucyl-tRNA, leucyl-tRNA, tyrosyl-tRNA, lysyl-tRNA, or valyl-tRNA synthetases. In the presence of borrelidin (7 μg./ml.) the growth rate of the bacteria was halved, while the sp. activities of aspartokinase and homoserine dehydrogenase increased 4-6-fold; threonine deaminase activity remained unchanged, demonstrating the specificity of the derepression process. When E. coli were grown in the presence of threonine (100 μg./ml.) and borrelidin (21 μg./ml.), growth limitation was almost abolished but a 3-fold derepression of threonine-specific aspartokinase was still observed. Borrelidin inhibits threonyl-tRNA synthetase in vivo, thus limiting the production of threonine-charged RNA and leading to growth inhibition. Also, inhibition of threonyl-tRNA synthetase by borrelidin derepressed threonine biosynthetic enzymes, since the formation of repressor from threonine by the threonyl-tRNA synthetase was also impaired.

IT 7184-60-3
RL: BIOL (Biological study)
(threonine formation inhibition by)
RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

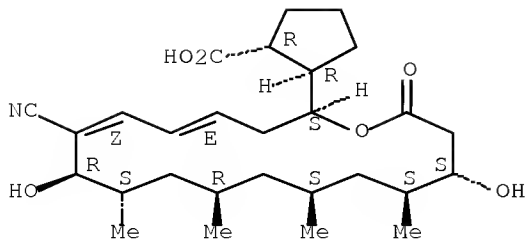
Absolute stereochemistry.
Double bond geometry as shown.



CC 8 (Microbial Biochemistry)
IT 7184-60-3
RL: BIOL (Biological study)
(threonine formation inhibition by)

L45 ANSWER 6 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2007:315049 HCAPLUS Full-text
DOCUMENT NUMBER: 146:513453
TITLE: Mutasynthesis - uniting chemistry and genetics for drug discovery
AUTHOR(S): Weissman, Kira J.
CORPORATE SOURCE: Department of Biochemistry, University of Cambridge, Cambridge, CB2 1GA, UK
SOURCE: Trends in Biotechnology (2007), 25(4), 139-142
CODEN: TRBIDM; ISSN: 0167-7799
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review. Mutasynthesis couples the power of chemical synthesis with mol. biol. to generate derivs. of medicinally valuable, natural products. Recently, this technique has been exploited by Cambridge-based biotech company Biotica Technol. Ltd, and their collaborators, to generate promising new variants of the polyketide anti-cancer compds. rapamycin and borrelidin.
IT 7184-60-3P, Borrelidin
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(mutasynthesis - uniting chemical and genetics for drug discovery)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 1-0 (Pharmacology)
IT 7184-60-3P, Borrelidin 53123-88-9P, Rapamycin
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(mutasynthesis - uniting chemical and genetics for drug discovery)
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 7 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1256641 HCAPLUS Full-text
DOCUMENT NUMBER: 146:50262
TITLE: Antibiotic kit and compositions
INVENTOR(S): Friedman, Doron; Besonov, Alex; Tamarkin, Dov; Eini, Meir
PATENT ASSIGNEE(S): Foamix Ltd., Israel
SOURCE: U.S. Pat. Appl. Publ., 31pp., Cont.-in-part of U.S. Ser. No. 532,618.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 28
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060269485	A1	20061130	US 2006-448490	20060607
WO 2004037225	A2	20040506	WO 2003-IB5527	20031024
WO 2004037225	A3	20041229		
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US 20050069566	A1	20050331	US 2004-911367	20040804
US 20060140984	A1	20060629	US 2005-532618	20051222
AU 2006339311	A2	20070907	AU 2006-339311	20060607
AU 2006339311	A1	20070907		
CA 2611577	A1	20070907	CA 2006-2611577	20060607
WO 2007099396	A2	20070907	WO 2006-IB3975	20060607
WO 2007099396	A3	20080313		
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EP 1919449 A2 20080514 EP 2006-847249 20060607
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US 20070292355 A1 20071220 US 2007-732547 20070404

WO 2008075207 A2 20080626 WO 2007-IB4459 20070404
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BY, KG, KZ, MD, RU, TJ, TM

IN 2007KN04925 A 20080704 IN 2007-KN4925 20071218

PRIORITY APPLN. INFO.:

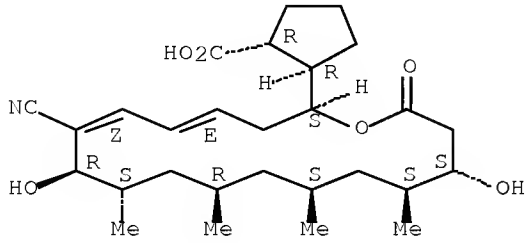
US 2002-429546P	P	20021129
US 2003-492385P	P	20030804
WO 2003-IB5527	W	20031024
US 2004-911367	A2	20040804
US 2005-688244P	P	20050607
US 2005-532618	A2	20051222
IL 2002-152486	A	20021025
US 2003-497648P	P	20030825
US 2003-530015P	P	20031216
US 2004-835505	A2	20040428
US 2004-922358	A2	20040820
US 2005-41921	A2	20050124
US 2006-789186P	P	20060404
US 2006-448490	A2	20060607
WO 2006-IB3975	W	20060607
US 2006-861620P	P	20061129
US 2007-880434P	P	20070112

AB The present invention relates to a therapeutic kit to provide an effective dosage of an antibiotic including an aerosol packaging assembly. The assembly includes a container accommodating a pressurized product; and an outlet capable of releasing the pressurized product as a foam, wherein the pressurized product comprises a foamable composition of an antibiotic; at least one organic carrier selected from the group consisting of a hydrophobic organic carrier, an organic polar solvent, an emollient and mixts. at 2-50%, a surfactant, 0.01-5% by weight of at least one polymeric additive selected from the group consisting of a bioadhesive agent, a gelling agent, a film forming agent and a phase change agent, water; and liquefied or compressed gas propellant at 3-25% by weight of the total composition

IT 7184-60-3, Treponemycin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antibiotic kit and compns.)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



INCL 424045000
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 1, 62
IT 6833-84-7, Nonactin 6834-98-6, Pentamycin 6980-18-3, Kasugamycin 6990-06-3, Fusidic acid 6990-06-3D, Fusidic acid, derivs. 6998-60-3, Rifamycin 7177-48-2, Ampicillin trihydrate 7184-60-3, Treponemycin 7229-50-7, Streptolydigin 7440-22-4, Silver, biological studies 7440-44-0, Carbon, biological studies 7542-37-2, Catenulin 7553-56-2, Iodine, biological studies 7631-86-9, Silicon oxide, biological studies 7681-93-8, Natamycin 7722-84-1, Hydrogen peroxide, biological studies 7761-88-8, Silver nitrate, biological studies 7778-54-3, Calcium hypochlorite 7782-44-7, Oxygen, biological studies 7783-96-2, Silver iodide 7783-97-3, Silver iodate 8025-81-8, Foromacidin 8044-71-1, Cetrimide 8064-90-2, Sulfamethoxazole-trimethoprim mixture 8065-41-6, Aureofungin 9000-07-1, Carrageenan gum 9000-30-0, Guar gum 9000-40-2, Locust bean gum 9000-65-1, Tragacanth gum 9001-63-2, Lysozyme 9004-30-2, Hydroxyethylcarboxymethylcellulose 9004-32-4, Carboxymethylcellulose 9004-62-0, Hydroxyethyl cellulose 9004-64-2, Hydroxypropyl cellulose 9004-65-3, Hydroxypropyl methylcellulose 9004-67-5, Methylcellulose 9008-54-2, Circulin 9008-55-3, Coliformin 9014-02-2, Neocarcinostatin 9032-42-2, Methylhydroxyethylcellulose 10023-07-1, Frenolicin 10118-90-8, Minocycline 10233-03-1, Magnesium hypochlorite 11003-33-1, Bleomycin B 11003-38-6, Capreomycin 11005-09-7, Phytoactin 11005-96-2, Danomycin 11005-98-4, Destomycin B 11006-22-7, Flavofungin 11006-33-0, Phleomycin 11006-64-7, Iyomycin 11006-70-5, Olivomycin 11006-76-1, Mikamycin 11006-83-0, Thermorubin 11011-72-6, Bluensomycin 11014-70-3, Levorin 11015-37-5, Moenomycin 11016-07-2, Perimycin 11016-19-6, Phytostreptin 11016-29-8, Polcillin 11016-71-0, Rubiflavin 11016-72-1, Rubomycin 11017-43-9, Siomycin 11021-88-8, Venturicidin 11030-68-5, Desdamethine 11031-38-2, Rubradirin 11031-48-4, Sarkomycin 11032-08-9, Thermothiocin 11033-34-4, Steffimycin 11043-99-5, Mitomalcin 11048-13-8, Nebramycin 11048-97-8, Hedamycin 11051-71-1, Avilamycin 11052-01-0, Ericamycin 11054-63-0, Tsushimycin 11056-20-5, Zorbamycin 11075-36-8, Tuberactinomycin 11078-21-0, Filipin 11078-23-2, Copiamycin 11079-53-1, Hyperforin 11089-65-9, Tunicamycin 11096-49-4, Partricin 11111-12-9, Cephalosporin 11111-23-2, Lividomycin 11113-62-5, Enniatin 11113-64-7, Imanine

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12001-79-5, Vitamin K 12001-79-5D, Vitamin K, derivs. 12609-84-6,
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12633-72-6D, Amphotericin, Me derivs. 12634-34-3, Macromomycin
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12772-35-9, Butirosin 13058-67-8, Lucensomycin 13182-89-3,
Metronidazole benzoate 13292-46-1, Rifampicin 13410-30-5,
6-Azathymidine 13463-67-7, Titanium dioxide, biological studies
13614-98-7, Minocycline hydrochloride 13838-08-9, Azidamfenicol
13929-35-6, Nancimycin 13929-35-6D, Nancimycin, derivs. 14698-29-4,
Oxolinic acid 14807-96-6, Talc, biological studies 14918-35-5,
Destomycin A 15318-45-3, Thiamphenicol 15387-18-5, Fezatione
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16887-00-6, Perchloride, biological studies 17090-79-8, Monensin
17243-38-8, Azidocillin 17397-89-6, Cerulenin 17650-86-1, Amicetin
18268-45-6, Silver laurate 18323-44-9, Clindamycin 18472-51-0,
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Siccanin 22832-87-7, Miconazole nitrate 22862-76-6, Anisomycin
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23155-02-4, Fosfomycin 23214-92-8, Doxorubicin 23239-41-0
23363-64-6, Chlorflavonin 23477-98-7, Sedecamycin 23510-81-8, Humulone
23593-75-1, Clotrimazole 23668-11-3, Pactamycin 24168-96-5,
Isoconazole nitrate 24169-02-6, Econazole nitrate 24394-09-0, Cnicin
24751-69-7, Nucleocidin 25265-75-2, Butylene glycol 25316-40-9,
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27726-31-4 28002-70-2, Framycetin sulfate 28069-65-0, Cuprimyxin
28399-50-0, Rabelomycin 28657-80-9, Cinoxacin 28978-07-6, Anticapsin
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31282-04-9, Hygromycin B 31692-85-0, Glycofurol 32385-11-8, Sisomicin
32886-97-8, Pivmecillinam 32887-01-7, Mecillinam 32887-03-9,
Pivmecillinam hydrochloride 32986-56-4, Tobramycin 32988-50-4
33817-20-8, Pivampicillin 34051-04-2, 3'-Deoxyneamine 34291-03-7,
Butirosin B 34444-01-4, Cefamandole 34493-98-6, Dibekacin
34642-77-8, Amoxicillin sodium 34787-01-4, Ticarcillin 35025-95-7,
3',4'-Dideoxyneamine 35457-80-8, Midecamycin 35531-88-5, Carindacillin
35554-44-0, Enilconazole 35607-66-0, Cefoxitin 35663-85-5,
Cyclamidomycin 35818-31-6, Cladosporin 35818-32-7, Monomethyl
cladosporin 35818-33-8, Monoacetyl cladosporin 35834-26-5, Rosaramicin
35846-53-8, Maytansine 35865-33-9, Dianemycin 35891-70-4, Myriocin
36653-82-4, Cetyl alcohol 37065-29-5, Miloxacin 37091-66-0, Azlocillin
37217-63-3 37217-65-5, Candimycin 37231-28-0, Melittin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antibiotic kit and compns.)

L45 ANSWER 8 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:1176162 HCAPLUS Full-text
DOCUMENT NUMBER: 145:470057
TITLE: Process for the preparation of L-threonine using bacteria of the Enterobacteriaceae family
INVENTOR(S): Kruse, Daniela; Hermann, Thomas; Thierbach, Georg; Rieping, Mechthild
PATENT ASSIGNEE(S): Degussa AG, Germany
SOURCE: U.S. Pat. Appl. Publ., 25pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 20060252133	A1	20061109	US 2006-566606	20060511
WO 2005014842	A1	20050217	WO 2004-EP8390	20040727

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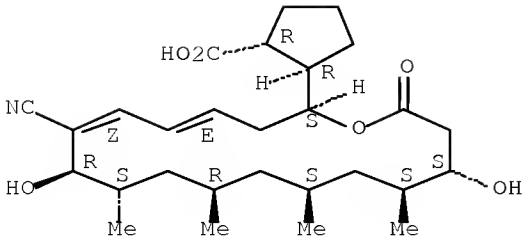
PRIORITY APPLN. INFO.:

DE 2003-10335253	A	20030801
US 2003-491981P	P	20030804
DE 2004-102004230552A		20040511
DE 2004-102004288593A		20040615
WO 2004-EP8390	W	20040727
DE 2004-102004023055A		20040511
DE 2004-102004028859A		20040615

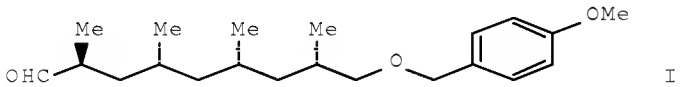
AB The invention relates to an improved process for the fermentative preparation of L-threonine using bacteria of the Enterobacteriaceae family which produce L-threonine.
IT 7184-60-3, Borrelidin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resistance to; process for preparation of L-threonine using bacteria of Enterobacteriaceae family)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



INCL 435106000; 435252330
CC 16-2 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 3
IT 56-84-8, L-Aspartic acid, biological studies 56-86-0, L-Glutamic acid, biological studies 56-87-1, L-Lysine, biological studies 98-83-9, α-Methylstyrene, biological studies 921-52-8, Diaminosuccinic acid 7184-60-3, Borrelidin 13292-46-1, Rifampicin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(resistance to; process for preparation of L-threonine using bacteria of Enterobacteriaceae family)

L45 ANSWER 9 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2006:937808 HCAPLUS Full-text
DOCUMENT NUMBER: 145:471283
TITLE: o-DPPB-directed copper-mediated allylic substitution: Part 2; Iterative deoxypropionate synthesis based on a copper-mediated directed allylic substitution: formal total synthesis of borrelidin (C3-C11 fragment)
AUTHOR(S): Herber, Christian; Breit, Bernhard
CORPORATE SOURCE: Inst. Org. Chem. Biochem., Albert-Ludwigs-Univ. Freiburg, Freiburg, 79104, Germany
SOURCE: Chemistry--A European Journal (2006), 12(25), 6684-6691
CODEN: CEUJED; ISSN: 0947-6539
PUBLISHER: Wiley-VCH Verlag GmbH & Co. KGaA
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 145:471283
GI



I

AB A new iterative strategy for the flexible preparation of any oligodeoxypropionate stereoisomer is presented which relies on an o-DPPB-directed copper-mediated allylic substitution employing enantiomerically pure Grignard reagents. This key C-C bond-forming step features reversed polarity compared with established enolate alkylation methodol. It thus avoids existing problems of enolate alkylation strategies such as enolate reactivity as well as costs and problems associated with the chiral auxiliary. Practicability of this new method is demonstrated through application in

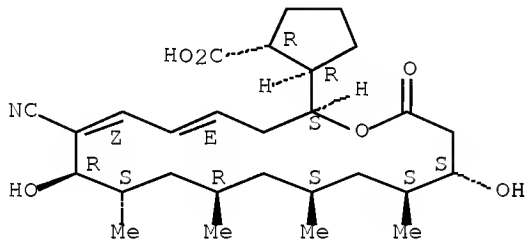
natural product syntheses. Thus, an efficient synthesis of the northern part of the angiogenesis inhibitor borrelidin, the deoxypropionate building block I, could be devised, representing a formal total synthesis.

IT 7184-60-3P
RL: PNU (Preparation, unclassified); PREP (Preparation)
(iterative deoxypropionate synthesis based on a copper-mediated directed allylic substitution and the formal total synthesis of borrelidin)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 23

ST deoxypropionate asym synthesis copper mediated allylic substitution Grignard Umpolung; formal synthesis polyketide borrelidin

IT Polyketides
RL: PNU (Preparation, unclassified); PREP (Preparation)
(iterative deoxypropionate synthesis based on a copper-mediated directed allylic substitution and the formal total synthesis of borrelidin)

IT 7184-60-3P
RL: PNU (Preparation, unclassified); PREP (Preparation)
(iterative deoxypropionate synthesis based on a copper-mediated directed allylic substitution and the formal total synthesis of borrelidin)

REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 10 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:141256 HCAPLUS Full-text
DOCUMENT NUMBER: 142:238754
TITLE: Fermentative preparation of L-threonine using recombinant Escherichia coli
INVENTOR(S): Kruse, Daniela; Hermann, Thomas; Thierbach, Georg; Rieping, Mechthild
PATENT ASSIGNEE(S): Degussa A.-G., Germany
SOURCE: PCT Int. Appl., 62 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005014843	A2	20050217	WO 2004-EP8470	20040729
WO 2005014843	A3	20050519		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 102004029639	A1	20050324	DE 2004-102004029639	20040618
EP 1654376	A2	20060510	EP 2004-741310	20040729
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1833028	A	20060913	CN 2004-80022849	20040729
BR 2004013562	A	20061017	BR 2004-13562	20040729
US 20070092950	A1	20070426	US 2006-567749	20060210
PRIORITY APPLN. INFO.:			DE 2003-10337028 A	20030812
			US 2003-494566P P	20030813
			DE 2004-102004029639A	20040618
			WO 2004-EP8470 W	20040729

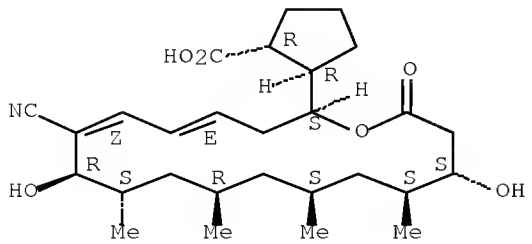
AB The invention provides an improved process for the fermentative preparation of L-threonine using L-threonine-producing bacteria from the family Enterobacteriaceae. In particular, the invention provides a recombinant strain of Escherichia coli in which a threonine-insensitive aspartate kinase gene (thrA) is overexpressed and the rpoS gene is attenuated by inserting a stop codon into it coding sequence. Addnl., the invention provides a fed-batch or repeat-batch fermentation process for the production of L-threonine.

IT 7184-60-3, Borrelidin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fermentative preparation of L-threonine using recombinant Escherichia coli)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IC ICM C12P013-08

CC 16-2 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 3
IT 56-84-8, L-Aspartic acid, biological studies 56-86-0, L-Glutamic acid, biological studies 56-87-1, L-Lysine, biological studies 63-68-3, L-Methionine, biological studies 433-48-7, Fluoropyruvic acid 921-52-8, Diaminosuccinic acid 922-54-3 5424-29-3, α-Methylserine 7184-60-3, Borrelidin 13292-46-1, Rifampin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fermentative preparation of L-threonine using recombinant Escherichia coli)

L45 ANSWER 11 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:141255 HCAPLUS Full-text
DOCUMENT NUMBER: 142:238753
TITLE: Fermentative preparation of L-threonine using recombinant Escherichia coli
INVENTOR(S): Kruse, Daniela; Hermann, Thomas; Thierbach, Georg; Rieping, Mechthild
PATENT ASSIGNEE(S): Degussa A.-G., Germany
SOURCE: PCT Int. Appl., 67 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005014842	A1	20050217	WO 2004-EP8390	20040727
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 102004028859	A1	20050224	DE 2004-102004028859	20040615
EP 1649033	A1	20060426	EP 2004-763525	20040727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK				
CN 1829801	A	20060906	CN 2004-80021728	20040727
BR 2004013139	A	20061003	BR 2004-13139	20040727
US 20060252133	A1	20061109	US 2006-566606	20060511
PRIORITY APPLN. INFO.:			DE 2003-10335253 A	20030801
			US 2003-491981P P	20030804
			DE 2004-102004023055A	20040511
			DE 2004-102004028859A	20040615
			DE 2004-102004230552A	20040511
			DE 2004-102004288593A	20040615
			WO 2004-EP8390 W	20040727

AB The invention provides an improved process for the fermentative preparation of L-threonine using L-threonine-producing bacteria from the family Enterobacteriaceae. In particular, the invention provides a recombinant strain of Escherichia coli in which a threonine-insensitive aspartate kinase gene (thrA) is overexpressed and the rpoS gene is attenuated by inserting a

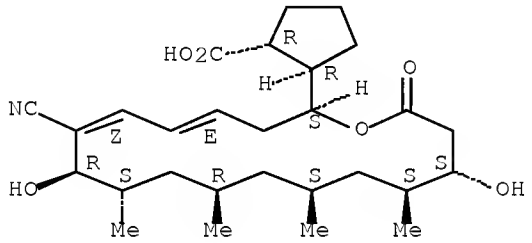
stop codon into it coding sequence. Addnl., the invention provides a fed-batch or repeat-batch fermentation process for the production of L-threonine.

IT 7184-60-3, Borrelidin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fermentative preparation of L-threonine using recombinant Escherichia coli)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IC ICM C12P013-08
ICS C12R001-19

CC 16-2 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 3

IT 56-84-8, L-Aspartic acid, biological studies 56-86-0, L-Glutamic acid, biological studies 56-87-1, L-Lysine, biological studies 63-68-3, L-Methionine, biological studies 433-48-7, Fluoropyruvic acid 921-52-8, Diaminosuccinic acid 922-54-3 5424-29-3, α-Methylserin 7184-60-3, Borrelidin 13292-46-1, Rifampin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fermentative preparation of L-threonine using recombinant Escherichia coli)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 12 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2005:141254 HCAPLUS Full-text
DOCUMENT NUMBER: 142:238752
TITLE: Fermentative preparation of L-threonine using recombinant Escherichia coli using a cell-recycle fermentor
INVENTOR(S): Kruse, Daniela; Hermann, Thomas; Rieping, Mechthild; Thierbach, Georg
PATENT ASSIGNEE(S): Degussa A.-G., Germany
SOURCE: PCT Int. Appl., 74 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 2005014841 A1 20050217 WO 2004-EP8389 20040727
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
DE 102004029340 A1 20050224 DE 2004-102004029340 20040617
EP 1649032 A1 20060426 EP 2004-763524 20040727
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, FI, RO, CY, TR, BG, CZ, EE, HU, PL, SK
PRIORITY APPLN. INFO.: DE 2003-10335254 A 20030801
US 2003-491982P P 20030804
DE 2004-102004029340A 20040617
WO 2004-EP8389 W 20040727

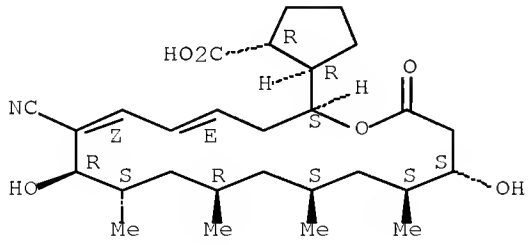
AB The invention provides an improved process for the fermentative preparation of L-threonine using L-threonine-producing bacteria from the family Enterobacteriaceae. In particular, the invention provides a recombinant strain of Escherichia coli in which a threonine-insensitive aspartate kinase gene (thrA) is overexpressed and the rpoS gene is attenuated by inserting a stop codon into it coding sequence. Addnl., the invention provides a fed-batch or repeat-batch fermentation process for the production of L-threonine using a cell-recycle fermentor.

IT 7184-60-3, Borrelidin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fermentative preparation of L-threonine using recombinant Escherichia coli using cell-recycle fermentor)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IC ICM C12P013-08
ICS C12R001-19

CC 16-2 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 3

IT 56-84-8, L-Aspartic acid, biological studies 56-86-0, L-Glutamic acid, biological studies 56-87-1, L-Lysine, biological studies 63-68-3, L-Methionine, biological studies 433-48-7, Fluoropyruvic acid

921-52-8, Diaminosuccinic acid 922-54-3 5424-29-3, α-Methylserin
7184-60-3, Borrelidin 13292-46-1, Rifampin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(fermentative preparation of L-threonine using recombinant Escherichia coli using cell-recycle fermentor)
REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 13 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2004:801181 HCAPLUS Full-text
DOCUMENT NUMBER: 141:271534
TITLE: Remedies and/or preventives for Plasmodium infection containing borrelidin
INVENTOR(S): Omura, Satoru; Otoguro, Kazuhiko; Yamada, Haruki; Ui, Hideaki
PATENT ASSIGNEE(S): Kitasato Institute, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 13 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

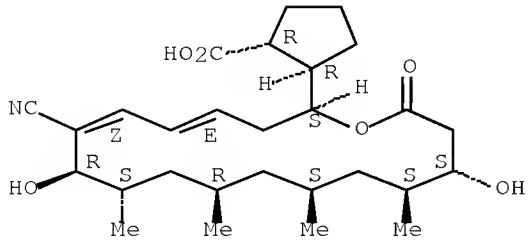
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2004269440	A	20040930	JP 2003-63769	20030310

PRIORITY APPLN. INFO.: JP 2003-63769 20030310

AB The invention provides remedies and/or preventives for Plasmodium infection caused by Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, and Plasmodium ovale, etc., wherein the agent is characterized by containing borrelidin as an active component. The antimalarial effect of borrelidin against drug resistant Plasmodium yoelii NS in mice was examined

IT 7184-60-3, Borrelidin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(remedies and/or preventives for Plasmodium infection containing borrelidin)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IC ICM A61K031-365
ICS A61P033-06; C07D313-00; C12P017-08

CC 1-5 (Pharmacology)
Section cross-reference(s): 63
IT 7184-60-3, Borrelidin
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(remedies and/or preventives for Plasmodium infection containing borrelidin)

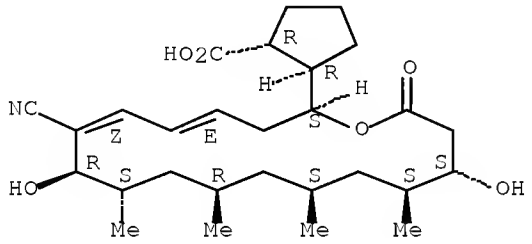
L45 ANSWER 14 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:256479 HCAPLUS Full-text
DOCUMENT NUMBER: 136:278229
TITLE: Escherichia mutants expressing chromosome-inserted thrABC operon from non-native promoter and their use in threonine production
INVENTOR(S): Liaw, Hungming James; Bradshaw, Jill S.; Yang, Yueqin; Mao, Weiying
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 92 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002026993	A1	20020404	WO 2001-US30558	20010928
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 20020106800	A1	20020808	US 2001-962303	20010926
US 7220571	B2	20070522		
CA 2423870	A1	20020404	CA 2001-2423870	20010928
AU 2001096415	A	20020408	AU 2001-96415	20010928
EP 1322765	A1	20030702	EP 2001-977282	20010928
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
BR 2001014101	A	20061114	BR 2001-14101	20010928
AU 2001296415	B2	20070104	AU 2001-296415	20010928
MX 2003PA02683	A	20030910	MX 2003-PA2683	20030327
US 20070254337	A1	20071101	US 2007-786818	20070413
US 20080166788	A1	20080710	US 2008-51064	20080319
PRIORITY APPLN. INFO.:			US 2000-235884P	P 20000928
			US 2001-962303	A3 20010926
			WO 2001-US30558	W 20010928
			US 2007-786818	A3 20070413

AB Escherichia coli, containing a thrABC operon under control of a non-native promoter (such as tac) inserted into the chromosome, and the use of these E. coli strains for the fermentative production of threonine are disclosed. Addnl., the thrA gene may encode a feedback-resistant aspartate kinase-homoserine dehydrogenase, or the E. coli may be mutated to resistance to threonine raffinate, borrelidin, or cyclopentanecarboxylic acid. One such recombinant E. coli produced 96.2 g L-threonine/L in fermentor culture (relative to the parent strain which produced 5.1 g/L).

IT 7184-60-3, Borrelidin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(E. coli resistant to; escherichia mutants expressing chromosome-inserted thrABC operon from non-native promoter and their use in threonine production)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IC ICM C12N015-52
ICS C12P013-08
CC 16-2 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 3, 10
IT 3400-45-1, Cyclopentanecarboxylic acid 7184-60-3, Borrelidin
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(E. coli resistant to; escherichia mutants expressing chromosome-inserted thrABC operon from non-native promoter and their use in threonine production)
REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 15 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2002:172047 HCAPLUS Full-text
DOCUMENT NUMBER: 136:215515
TITLE: Fermentation of L-threonine with transgenic microorganisms carrying the thrABC operon
INVENTOR(S): Hermann, Thomas; Rieping, Mechthild
PATENT ASSIGNEE(S): Degussa AG, Germany
SOURCE: PCT Int. Appl., 39 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002018543	A2	20020307	WO 2001-EP8603	20010725
WO 2002018543	A3	20030103		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT,

RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

DE 10103778	A1	20020314	DE 2001-10103778		20010127
AU 2002020542	A	20020313	AU 2002-20542		20010725
EP 1313838	A2	20030528	EP 2001-984568		20010725
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
CN 1630711	A	20050622	CN 2001-814966		20010725
MX 2003PA00585	A	20030606	MX 2003-PA585		20030120
ZA 2003001636	A	20040203	ZA 2003-1636		20030227
PRIORITY APPLN. INFO.:			DE 2000-10042745	A	20000831
			DE 2001-10103778	A	20010127
			WO 2001-EP8603	W	20010725

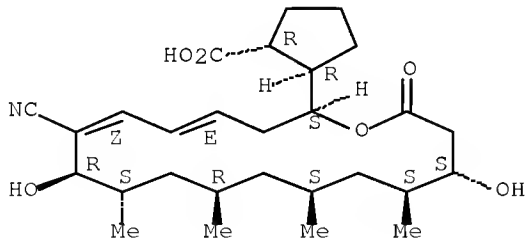
AB The invention relates to a process for the fermentative preparation of L-threonine in which an L-threonine-producing microorganism of the Enterobacteriaceae family is cultured by the feed process, and a portion of the fermentation broth is then separated off in order to be utilized for inoculation of further media. The use of the thrABC to increase the levels of enzymes of threonine biosynthesis is demonstrated. The parB gene is used to stabilize the plasmid carrying the thrABC operon. Strains are also resistant to the adverse effects of high concns. of threonine. The space-time yield of threonine from transgenic Escherichia coli was up to 1.94 g/L+h compared to 1.76 g/L+h for the parental strain.

IT 7184-60-3, Borrelidin
RL: BSU (Biological study, unclassified); BIOL (Biological study) (resistance to, in threonine-fermenting microorganisms; fermentation of L-threonine with transgenic microorganisms carrying thrABC operon)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IC ICM C12N001-21
ICS C12P013-08; C12N001-21; C12R001-19

CC 16-2 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 3, 10

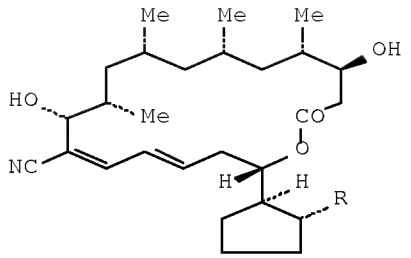
IT 56-86-0, L-Glutamic acid, biological studies 921-52-8, Diaminosuccinic acid 5424-29-3, α-Methylserine 7184-60-3, Borrelidin
RL: BSU (Biological study, unclassified); BIOL (Biological study) (resistance to, in threonine-fermenting microorganisms; fermentation of L-threonine with transgenic microorganisms carrying thrABC operon)

L45 ANSWER 16 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 2001:101120 HCAPLUS Full-text
DOCUMENT NUMBER: 134:147437
TITLE: Preparation of borrelidin derivatives for pharmaceutical use as angiogenesis inhibiting agents
INVENTOR(S): Makk, Nandor; Ambrus, Gabor; Tegdes, Aniko; Jeney, Andras; Timar, Ferenc
PATENT ASSIGNEE(S): Gyogyszerkutato Intezet Kft., Hung.
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001009113	A2	20010208	WO 2000-HU88	20000802
WO 2001009113	A3	20010614		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
HU 9902628	A2	20010528	HU 1999-2628	19990802
HU 9902628	A3	20010730		
CA 2378176	A1	20010208	CA 2000-2378176	20000802
BR 2000012968	A	20020514	BR 2000-12968	20000802
EP 1206462	A2	20020522	EP 2000-949831	20000802
EP 1206462	B1	20030528		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
HU 2002002197	A2	20021028	HU 2002-2197	20000802
HU 2002002197	A3	20051128		
JP 2003506366	T	20030218	JP 2001-514316	20000802
AT 241611	T	20030615	AT 2000-949831	20000802
PT 1206462	T	20031031	PT 2000-949831	20000802
ES 2200900	T3	20040316	ES 2000-949831	20000802
AU 772206	B2	20040422	AU 2000-63090	20000802
NZ 517422	A	20050225	NZ 2000-517422	20000802
RU 2247723	C2	20050310	RU 2002-105518	20000802
AP 1383	A	20050405	AP 2002-2413	20000802
NO 2002000485	A	20020321	NO 2002-485	20020130
ZA 2002000838	A	20030605	ZA 2002-838	20020130
IN 2002CN00148	A	20050311	IN 2002-CN148	20020130
BG 106373	A	20020930	BG 2002-106373	20020131
MX 2002PA01117	A	20030820	MX 2002-PA1117	20020131
HR 2002000103	B1	20050630	HR 2002-103	20020201
US 6815465	B1	20041109	US 2002-48659	20020603
HK 1048995	A1	20060721	HK 2003-101165	20030218

PRIORITY APPLN. INFO.: HU 1999-2628 A 19990802
WO 2000-HU88 W 20000802

OTHER SOURCE(S): MARPAT 134:147437
GI



I

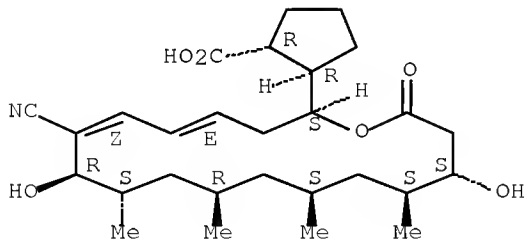
AB Borrelidin derivs., such as I [R = -COOR1, -CONR2R3, -CONR4CONR4R5 or -CH2OR6; R1 = alkyl, cycloalkyl; R2, R3 = H, alkyl, cycloalkyl, heteroaryl; R4, R5 = H, alkyl, cycloalkyl, phenyl; R6 = H, alkyl, cycloalkyl, Ph, carbamoyl, benzoyl, alkylsulfonyl], were prepared to inhibit the neovascularization in living tissues and as such can be used for preventing and inhibiting angiogenesis appearing in connection with tumor growth and for preventing the formation of tumor metastases. Thus, I [R = -CO2(CH2)2R1, R1 = 4-morpholinyl] was prepared by esterifying borrelidin with 4-(2-hydroxyethyl)morpholine using 1-hydroxybenzotriazole, 4-dimethylaminopyridine and dicyclohexylcarbodiimide in THF. The prepared borrelidin derivs. were tested for angiogenesis inhibiting activity.

IT 7184-60-3, Borrelidin
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of borrelidin derivs. for pharmaceutical use as angiogenesis inhibiting agents)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IC ICM C07D313-00
ICS C07D405-12; A61K031-335; A61P035-00

CC 26-6 (Biomolecules and Their Synthetic Analogs)
Section cross-reference(s): 1

IT 100-46-9, Benzenemethanamine, reactions 103-74-2, 2-Pyridineethanol 108-91-8, Cyclohexanamine, reactions 141-43-5, reactions 462-08-8, 3-Pyridinamine 617-89-0, 2-Furanmethanamine 622-40-2, 4-Morpholineethanol 2038-03-1, 4-Morpholineethanamine 2387-23-7 3731-51-9, 2-Pyridinemethanamine 3731-52-0, 3-Pyridinemethanamine

3731-53-1, 4-Pyridinemethanamine 7184-60-3, Borrelidin
27532-96-3
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of borrelidin derivs. for pharmaceutical use as angiogenesis inhibiting agents)

L45 ANSWER 17 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1998:106028 HCAPLUS Full-text
DOCUMENT NUMBER: 128:179453
ORIGINAL REFERENCE NO.: 128:35415a,35418a
TITLE: Novel strains of Escherichia coli containing recombinant plasmids for improved production of L-threonine by fermentation
INVENTOR(S): Wang, Ming-Der; Bradshaw, Jill S.; Swisher, Stacia L.; Liaw, Hungming James; Hanke, Paul D.; Binder, Thomas P.
PATENT ASSIGNEE(S): Archer-Daniels-Midland Company, USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9804715	A1	19980205	WO 1997-US13359	19970730
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW				
RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
US 5939307	A	19990817	US 1997-902336	19970729
CA 2262813	A1	19980205	CA 1997-2262813	19970730
ZA 9706803	A	19980219	ZA 1997-6803	19970730
AU 9738994	A	19980220	AU 1997-38994	19970730
AU 730102	B2	20010222		
EP 917578	A1	19990526	EP 1997-936291	19970730
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1226931	A	19990825	CN 1997-196897	19970730
BR 9710503	A	20000111	BR 1997-10503	19970730
HU 9903856	A2	20000328	HU 1999-3856	19970730
NZ 334032	A	20000929	NZ 1997-334032	19970730
JP 2000515763	T	20001128	JP 1998-509111	19970730
RU 2212448	C2	20030920	RU 1999-104488	19970730
PL 191395	B1	20060531	PL 1997-331351	19970730
NO 9900362	A	19990126	NO 1999-362	19990126
NO 320044	B1	20051017		
KR 2000029691	A	20000525	KR 1999-700770	19990129
PRIORITY APPLN. INFO.:			US 1996-22407P P	19960730
			WO 1997-US13359 W	19970730

AB Disclosed is a strain of Escherichia coli containing in its chromosome a genetic determinant of amino acid biosynthesis, e.g., the threonine operon, under the control of a non-native promoter for the production of threonine. It does not require any recombinant plasmids containing genes that encode threonine biosynthetic enzymes to produce threonine. Optionally, amino acid

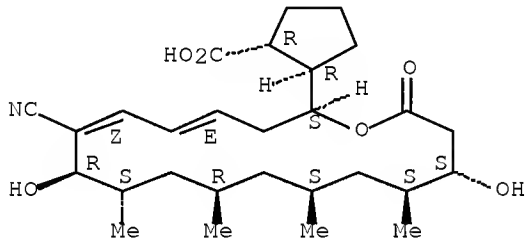
nutritional requirements for and/or regulatory hindrance to amino acid biosynthesis are removed from the chromosome. Preparation of Escherichia coli strains containing the threonine operon from E. coli strain ATCC 21277, the tac promoter, a defective threonine dehydrogenase gene, borrelidin resistance, etc. was demonstrated. Escherichia coli strain kat-13 produced 102 threonine g/L after 48-h fermentation

IT 7184-60-3, Borrelidin
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(resistance to; threonine high producer Escherichia coli strain containing in chromosome; novel strains of Escherichia coli without containing recombinant plasmids for improved production of L-threonine by fermentation)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



IC ICM C12N015-52
ICS C12P013-08; C12N015-70; C12N015-90; C12N001-21; C12N001-21; C12R001-19

CC 16-2 (Fermentation and Bioindustrial Chemistry)
Section cross-reference(s): 10

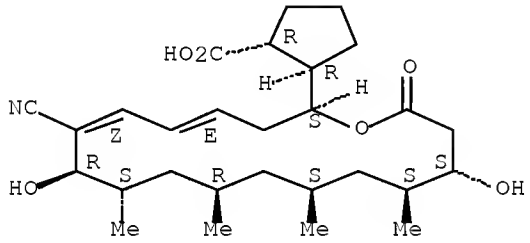
IT 7184-60-3, Borrelidin
RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
(resistance to; threonine high producer Escherichia coli strain containing in chromosome; novel strains of Escherichia coli without containing recombinant plasmids for improved production of L-threonine by fermentation)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L45 ANSWER 18 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1993:441918 HCAPLUS Full-text
DOCUMENT NUMBER: 119:41918
ORIGINAL REFERENCE NO.: 119:7483a,7486a
TITLE: Threonyl-tRNA synthetase gene amplification in borrelidin-resistant mammalian cells
AUTHOR(S): Arfin, Stuart M.; Gerken, Steven C.; Kontis, Kris J.; Cruzen, Matt E.
CORPORATE SOURCE: Univ. California, Irvine, CA, USA
SOURCE: Gene Amplif. Mamm. Cells (1993), 97-106. Editor(s): Kellems, Rodney E. Dekker: New York, N. Y.

CODEN: 58VCAS
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
AB A review with 15 refs on threonyl-tRNA synthetase gene amplification in response to the antibiotic borrelidin. Topics include: selection of borrelidin-resistant chinese hamster ovary cells; threonyl-tRNA synthetase activity, protein and mRNA levels, and gene copy number; regulation of threonyl-tRNA synthetase expression; and preliminary characterization of the threonyl-tRNA synthetase gene.
IT 7184-60-3, Borrelidin
RL: BIOL (Biological study)
(resistance to, threonyl-tRNA synthetase gene amplification for)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 3-0 (Biochemical Genetics)
Section cross-reference(s): 1
IT 7184-60-3, Borrelidin
RL: BIOL (Biological study)
(resistance to, threonyl-tRNA synthetase gene amplification for)

L45 ANSWER 19 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1992:52826 HCAPLUS Full-text
DOCUMENT NUMBER: 116:52826
ORIGINAL REFERENCE NO.: 116:9015a,9018a
TITLE: Four major transcriptional responses in the methionine/threonine biosynthetic pathway of Saccharomyces cerevisiae
AUTHOR(S): Mountain, Harry A.; Bystroem, Anders S.; Larsen, Joergen Tang; Korch, Christopher
CORPORATE SOURCE: Dep. Microbiol., Univ. Umea, Umea, S-901 87, Swed.
SOURCE: Yeast (1991), 7(8), 781-803
CODEN: YESTE3; ISSN: 0749-503X
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Genes encoding enzymes in the threonine/methionine biosynthetic pathway were cloned and used to investigate their transcriptional response to signals known to affect gene expression on the basis of enzyme specific-activities. Four major responses were evident: strong repression by methionine of MET3, MET5 and MET14, as previously described for MET3, MET2 and MET25; weak repression by methionine of MET6; weak stimulation by methionine but no response to threonine was seen for THR1, HOM2 and HOM3; no response to any of the signals

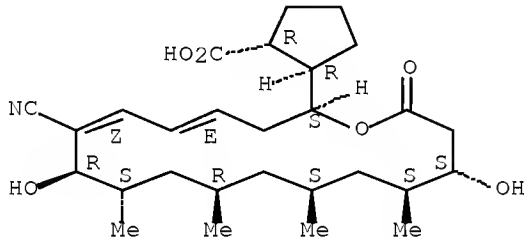
tested, for HOM6 and MES1. In a BOR3 mutant, THR1, HOM2 and HOM3 mRNA levels were increased slightly. The stimulation of transcription by methionine for HOM2, HOM3 and THR1 is mediated by the GCN4 gene product and hence these genes are under the general amino acid control. In addition to the strong repression by methionine, MET5 is also regulated by the general control.

IT 7184-60-3, Borrelidin
RL: BIOL (Biological study)
(BOR genes for resistance to, of Saccharomyces cerevisiae, methionine/threonine biosynthesis regulation in relation to)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 3-4 (Biochemical Genetics)
Section cross-reference(s): 10

IT Saccharomyces cerevisiae
(methionine/threonine biosynthesis genes of, transcription of)

IT Transcription, genetic
(of methionine/threonine biosynthesis genes of, Saccharomyces cerevisiae)

IT Molecular cloning
(of methionine/threonine biosynthetic pathway genes, of Saccharomyces cerevisiae)

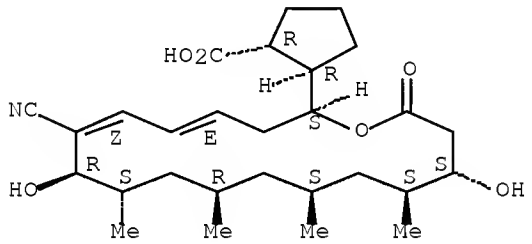
IT Genetic mapping
(restriction endonuclease, of methionine/threonine biosynthetic pathway genes, of yeast)

IT 7184-60-3, Borrelidin
RL: BIOL (Biological study)
(BOR genes for resistance to, of Saccharomyces cerevisiae, methionine/threonine biosynthesis regulation in relation to)

L45 ANSWER 20 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1989:402086 HCAPLUS Full-text
DOCUMENT NUMBER: 111:2086
ORIGINAL REFERENCE NO.: 111:411a,414a
TITLE: Isolation of a cDNA clone for human threonyl-tRNA synthetase: amplification of the structural gene in borrelidin-resistant cell lines
AUTHOR(S): Kontis, Kris J.; Arfin, Stuart M.
CORPORATE SOURCE: Coll. Med., Univ. California, Irvine, CA, 92717, USA
SOURCE: Molecular and Cellular Biology (1989), 9(5), 1832-8
CODEN: MCEBD4; ISSN: 0270-7306

DOCUMENT TYPE: Journal
LANGUAGE: English
AB A cDNA for threonyl-tRNA synthetase was isolated from a human placental cDNA λgt11 expression library by immunol. screening, and its identity was confirmed by hybrid-selected mRNA translation. With this cDNA used as a hybridization probe, borrelidin-resistant Chinese hamster ovary cells that overproduced threonyl-tRNA synthetase were shown to have increased levels of threonyl-tRNA synthetase mRNA and gene sequences. Amplification of the gene did not appear to have been accompanied by any major structural reorganizations.
IT 7184-60-3, Borrelidin
RL: PRP (Properties)
(CHO cells resistant to, human threonyl-tRNA synthetase mRNA formation in)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 3-4 (Biochemical Genetics)
Section cross-reference(s): 13
IT 7184-60-3, Borrelidin
RL: PRP (Properties)
(CHO cells resistant to, human threonyl-tRNA synthetase mRNA formation in)

L45 ANSWER 21 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1985:450922 HCAPLUS Full-text
DOCUMENT NUMBER: 103:50922
ORIGINAL REFERENCE NO.: 103:8151a,8154a
TITLE: Treponemycin, a nitrile antibiotic active against Treponema hyodysenteriae
AUTHOR(S): Singh, S. K.; Gurusiddaiah, S.; Whalen, J. W.
CORPORATE SOURCE: Bioanal. Cent., Washington State Univ., Pullman, WA, 99164, USA
SOURCE: Antimicrobial Agents and Chemotherapy (1985), 27(2), 239-45
CODEN: AMACCQ; ISSN: 0066-4804
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Two strains of Streptomyces (isolates 275 and 124) were isolated from soil samples. Based on their cellular morphol. and physiol., the 2 isolates were identified as S. albovinaceous. Both isolates produced an antibiotic when grown in liquid culture medium containing homogenized oats. The antibiotic, treponemycin (I), was isolated from the culture broth by solvent extraction

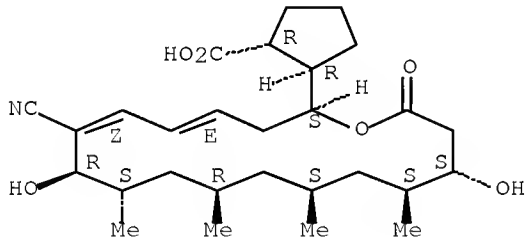
and purified by silica gel column and preparative TLC. I is a crystalline light-yellow compound, m.p. 93-5°, that is levorotatory and soluble in most organic solvents. It is sparingly soluble in water but insol. in petroleum ether. On the basis of elemental anal. and mass spectral data, its mol. formula was deduced to be C28H43O6N. IR spectra indicated the presence of unsatn., nitrile, lactone, ester, or all 3 functions, and carbonyl functions in I. A sharp IR absorption band for nitrile at 2220 cm-1 and the presence of an unsatd. group indicated that the nitrile function may be attached to an unsatd. C atom. The presence of dienenitrile functions was further supported by the UV absorption spectrum of the antibiotic, which gave a UVmax at 257 nm. The NMR spectrum did not give any peak which could be exchanged with D2O, an indication of the absence of carboxylic and hydroxyl functions in I. All of the functional groupings indicated by the IR and UV spectra were further confirmed by the 13C-NMR spectrum. A brief hydrogenation of I yielded a biol. active tetrahydro derivative, whereas extended hydrogenation produced an inactive primary amine. Mild alkaline hydrolysis and subsequent esterification of the antibiotic with diazomethane produced an inactive di-Me ester. Apparently both the nitrile and the lactone functions are essential for I to show antimicrobial activity. I inhibited several species of bacteria, especially T. hyodysenteriae, the causative agent of swine dysentery. In view of the oral 50% LD of 400 mg/kg and its low min. inhibitory concentration against 4 strains of T. hyodysenteriae, I may have value as a swine dysentery therapeutic.

IT 7184-60-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(from Streptomyces albovinaceous, anti- Treponema hyodysenteriae activity of)

RN 7184-60-3 HCAPLUS

CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



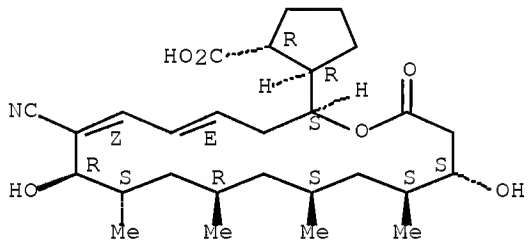
CC 10-1 (Microbial Biochemistry)
Section cross-reference(s): 1

IT 7184-60-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(from Streptomyces albovinaceous, anti- Treponema hyodysenteriae activity of)

L45 ANSWER 22 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1975:437367 HCAPLUS Full-text
DOCUMENT NUMBER: 83:37367

ORIGINAL REFERENCE NO.: 83:5859a,5862a
TITLE: Borrelidin
AUTHOR(S): Poralla, K.
CORPORATE SOURCE: Univ. Tuebingen, Tuebingen, Fed. Rep. Ger.
SOURCE: Antibiotics (1975), Volume 3, 365-9. Editor(s): Gottlieb, David; Shaw, Paul D.; Corcoran, John W. Springer: New York, N. Y.
CODEN: 19SYA8
DOCUMENT TYPE: Conference; General Review
LANGUAGE: English
GI For diagram(s), see printed CA Issue.
AB A review with 19 refs. discussing the antibiotic activity of borrelidin (I) [7184-60-3].
IT 7184-60-3
RL: BIOL (Biological study))
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 1-0 (Pharmacodynamics)
Section cross-reference(s): 3
IT 7184-60-3
RL: BIOL (Biological study)

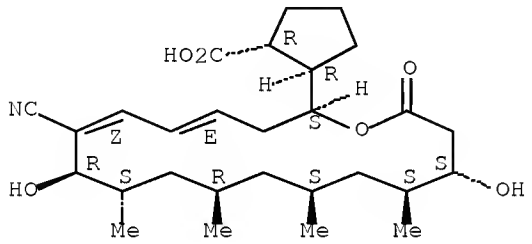
L45 ANSWER 23 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1974:433850 HCAPLUS Full-text
DOCUMENT NUMBER: 81:33850
ORIGINAL REFERENCE NO.: 81:5412h,5413a
TITLE: Microbial production of L-threonine. IV. Effect of the antibiotic, borrelidin, on the production of L-threonine by Escherichia coli auxotrophs
AUTHOR(S): Hirakawa, Tamotsu; Morinaga, Haruhiko; Watanabe, Kiyoshi
CORPORATE SOURCE: Biochem. Res. Lab., Kanegafuchi Chem. Ind. Co., Ltd., Takasago, Japan
SOURCE: Agricultural and Biological Chemistry (1974), 38(1), 85-9
CODEN: ABCHA6; ISSN: 0002-1369
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Borrelidin (I) [7184-60-3] greatly increased formation of L-threonine [72-19-5] by all 4 E. coli auxotrophs studied. Maximum yield of L-threonine (6.4 mg/ml) was observed with strain number 15 in the presence of 10 μg I/ml.

Sodium L-aspartate [17090-93-6] enhanced the effect of I on L-threonine formation. The maximum amount of L-threonine formed by E. coli strain number 234 in the presence of 5 mg sodium aspartate/ml and 10 μg I/ml was 50.0 mg/ml.

IT 7184-60-3
RL: PRP (Properties)
(threonine fermentation enhancement by, in Escherichia coli)

RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 3-2 (Biochemical Interactions)
Section cross-reference(s): 16

IT 7184-60-3
RL: PRP (Properties)
(threonine fermentation enhancement by, in Escherichia coli)

L45 ANSWER 24 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1974:66945 HCAPLUS Full-text
DOCUMENT NUMBER: 80:66945
ORIGINAL REFERENCE NO.: 80:10819a,10822a
TITLE: Electron-optical investigation of the effect of streptomycete's antibiotic borrelidin on the Pseudorabies virus
AUTHOR(S): Zoepel, P.; Eckardt, K.; Tonew, E. M.
CORPORATE SOURCE: Forschungszent. Molekularbiol. Med., Akad. Wiss., Jena, Ger. Dem. Rep.
SOURCE: Zeitschrift fuer Allgemeine Mikrobiologie (1973), 13(8), 711-22
CODEN: ZAPOAK; ISSN: 0044-2208
DOCUMENT TYPE: Journal
LANGUAGE: German

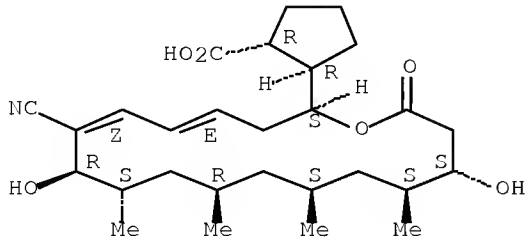
AB Electron micrographs of Pseudorabies virus replication in borrelidin (I) [7184-60-3] (2 and 5 μg/ml)-treated chicken embryonal fibroblasts (CEF) revealed an effect of I on the early steps of viral replication. Incomplete viral particles were found in the cytoplasm of I-treated CEF at a time when the regular viral replication cycle was finished in untreated control CEF. The artiviral activity of I probably depended on a blockade of the virus specific protein synthesis.

IT 7184-60-3
RL: PRP (Properties)
(pseudorabies virus replication inhibition by)

RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-

8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

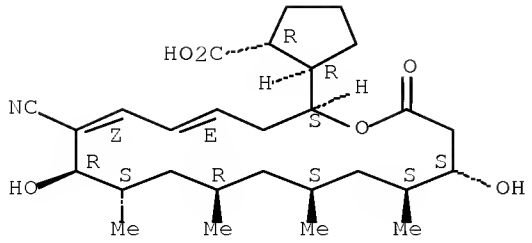
Absolute stereochemistry.
Double bond geometry as shown.



CC 3-2 (Biochemical Interactions)
IT 7184-60-3
RL: PRP (Properties)
(pseudorabies virus replication inhibition by)

L45 ANSWER 25 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1970:411565 HCAPLUS Full-text
DOCUMENT NUMBER: 73:11565
ORIGINAL REFERENCE NO.: 73:1917a,1920a
TITLE: Effect of borrelidin on the protein biosynthesis and the regulatory process in microorganisms
AUTHOR(S): Nass, Gisela
CORPORATE SOURCE: Max-Planck-Inst. Mol.-Genet., Berlin, Fed. Rep. Ger.
SOURCE: Zentralblatt fuer Bakteriologie, Parasitenkunde, Infektionskrankheiten und Hygiene, Abteilung 1: Medizinisch-Hygienische Bakteriologie, Virusforschung und Parasitologie, Originale (1970), 212(2-4), 239-45
CODEN: ZBPHA6; ISSN: 0372-8110
DOCUMENT TYPE: Journal
LANGUAGE: German
AB The antibiotic borrelidin (I) inhibits the enzymic activity of threonyl-tRNA synthetase (II) in Escherichia coli and yeast. Besides the inhibition of protein biosynthesis the action of I leads to a derepression of the formation of the threonine-biosynthetic enzymes in these cells, indicating that in single celled organisms (E. coli) as well as in more complex single celled organisms (yeast) II takes part in the repression of the threonine biosynthetic enzymes. The altered II activity in I-resistant E. coli mutants demonstrates the action of I on II.
IT 7184-60-3
RL: BIOL (Biological study)
(threonine formation derepression by, in microorganisms)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

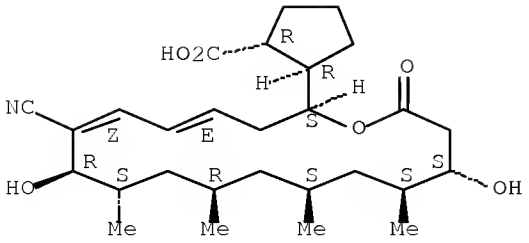
Absolute stereochemistry.
Double bond geometry as shown.



CC 8 (Microbial Biochemistry)
IT 7184-60-3
RL: BIOL (Biological study)
(threonine formation derepression by, in microorganisms)

L45 ANSWER 26 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1968:103621 HCAPLUS Full-text
DOCUMENT NUMBER: 68:103621
ORIGINAL REFERENCE NO.: 68:19987a,19990a
TITLE: Metabolic products of microorganisms. LXII. Inhibition of the attachment of threonine to sRNA in a cell-free system and of the synthesis of protein and nucleic acids in the cell by the antibiotic borrelidin
AUTHOR(S): Poralla, K.; Zaehner, Hans
CORPORATE SOURCE: Univ. Tuebingen, Tuebingen, Fed. Rep. Ger.
SOURCE: Archiv fuer Mikrobiologie (1968), 61, 143-53
CODEN: ARMKA7; ISSN: 0003-9276
DOCUMENT TYPE: Journal
LANGUAGE: German
AB Borrelidin specifically inhibited the attachment of L-threonine to soluble RNA at a concentration of 1.4 + 10-6M in a cell-free system of Bacillus subtilis. It did not inhibit the incorporation of L-isoleucine, L-valine, L-tyrosine, L-serine, L-glutamic acid, or L-proline. The macrolide antibiotics, lankamycin and erythromycin, at concns. 10-fold greater than required to inhibit growth, did not inhibit the binding of L-threonine or other amino acids to soluble RNA. In the cells, borrelidin (1.5 + 10-6M) inhibited the synthesis of protein, RNA, and DNA. Lankamycin and erythromycin selectively inhibited protein synthesis. Borrelidin is the first antibiotic known to block protein synthesis via inhibition of the incorporation of amino acids into soluble RNA. 32 references.
IT 7184-60-3
RL: BIOL (Biological study)
(inhibition of nucleic acids and protein formation by, in Bacillus subtilis)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

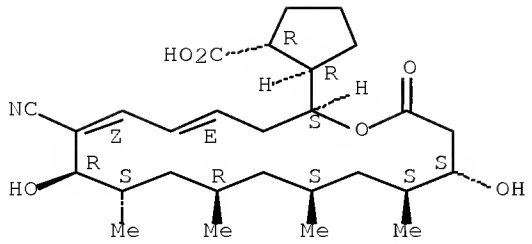
Absolute stereochemistry.
Double bond geometry as shown.



CC 15 (Pharmacodynamics)
IT 7184-60-3
RL: BIOL (Biological study)
(inhibition of nucleic acids and protein formation by, in Bacillus subtilis)

L45 ANSWER 27 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1965:405847 HCAPLUS Full-text
DOCUMENT NUMBER: 63:5847
ORIGINAL REFERENCE NO.: 63:1078b-d
TITLE: Antiviral activity of two antibiotics isolated from a species of Streptomyces
AUTHOR(S): Dickinson, Lois; Griffiths, A. J.; Mason, C. G.; Mills, R. F. N.
CORPORATE SOURCE: Boots Pure Drug Co., Ltd., Nottingham, UK
SOURCE: Nature (London, United Kingdom) (1965), 206(4981), 265-8
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Antiviral activity was shown against influenza virus, Newcastle disease virus, and vaccinia virus growing in chick embryo monolayers and against encephalomyocarditis virus growing in suspensions of Kreb's ascites tumor cells by liquors from Streptomyces C2989, but the liquors were inactive against bacteria. One of the liquors was injected intraperitoneally or subcutaneously into mice infected with encephalomyocarditis virus and found to markedly increase the number of animals that survived for 10 days. Borrelidin was found to be the inhibitor of in vitro virus growth, but it had no effect on the in vivo virus infections in mice. Another liquor from the culture of Streptomyces C2989 yielded vivomycin which was effective against the in vivo infections of encephalomyocarditis virus in mice if it was given intraperitoneally, intranasally, or subcutaneously, but not orally or intracerebrally. There was a synergistic effect obtained when vivomycin was given with borrelidin to mice infected with encephalomyocarditis virus or ascites tumor (against which neither had much activity alone) and against influenza virus in eggs. Vivomycin stimulated host defense mechanisms in a manner similar to that of endotoxins and like them is less toxic to mice than to dogs and rabbits.
IT 7184-60-3, Borrelidin
(as virucide)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

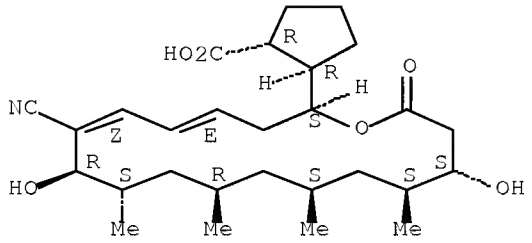


CC 68 (Pharmacodynamics)
IT 7184-60-3, Borrelidin
(as virucide)

L45 ANSWER 28 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1965:430867 HCAPLUS Full-text
DOCUMENT NUMBER: 63:30867
ORIGINAL REFERENCE NO.: 63:5448c-f
TITLE: Isolation of vivomycin and borrelidin, two antibiotics with antiviral activity, from a species of Streptomyces
AUTHOR(S): Lumb, M.; Macey, P. E.; Spyvee, J.; Whitmarsh, J. M.; Wright, R. D.
CORPORATE SOURCE: Boots Pure Drug Co., Ltd., Nottingham, UK
SOURCE: Nature (London, United Kingdom) (1965), 206(4981), 263-5
CODEN: NATUAS; ISSN: 0028-0836
DOCUMENT TYPE: Journal
LANGUAGE: English
AB cf. Dickinson, et al., CA 63, 1078b. Both antibacterial (especially against Corynebacterium) and antiviral activity was exhibited by the culture fluid of the organism. Maximum activity was reached after 96 hrs. of cultivation. The 1st antibiotic was found to be borrelidin (I) (Berger, et al., CA 44, 697a). It was extracted from culture fluids with BuOH or Me iso-Bu ketone, concentrated under vacuum, stirred with MeOH, decanted from the insol. fat, again concentrated under vacuum and precipitated with light petroleum to give 0.5 g./l. of broth, 10-20% pure. This material had high activity against C. xerosis and viruses in vitro, but no activity against encephalomyocarditis (EMC) virus in mice. The crude I (absolute maximum at 258 mμ) was concentrated by countercurrent extraction in water-MeOH-Me iso-Bu ketone-ligroine (5:5:2:8). Concentration and precipitation gave a colorless solid, m. 98-105°, containing 640 units/mg. It crystallized to colorless hexagonal plates from $CHCl_3$-CCl_4. The waste aqueous liquors contained another antibiotic, active in vivo but not in vitro. It was called vivomycin (II). It was produced maximally in the same culture after 48-60 hrs. incubation. I remaining in the broth was partially removed by acidifying to pH 2 and filtering; the remaining I was removed by washing with BuOH or Me iso-Bu ketone, or by absorbing the I and II from the neutralized liquor onto charcoal and eluting the II with 50% aqueous acetone. The crude solid II could be separated into a number of components by thin-layer chromatography with BuOH-HOAc-H_2O (12:3:5) and tert-BuOH-HOAc-H_2O (8:2:5). The most active component remained at the origin in the latter solvent. Purification on columns of G-25 and G-75 Sephadex gave a fibrous white solid, active against EMC virus in mice at 0.4-1.5 mg./kg. It appeared to be a polysaccharide containing about 48-55% arabinose, 16-21% galactose, and 22-31% glucose.
IT 7184-60-3P, Borrelidin

RL: PREP (Preparation)
(separation from vivomycin)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

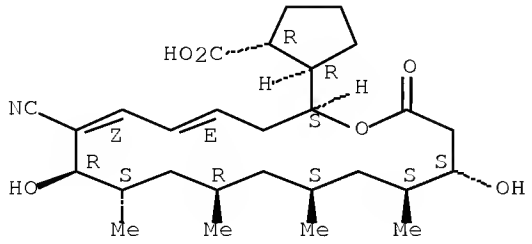


CC 30 (Pharmaceuticals)
IT 7184-60-3P, Borrelidin
RL: PREP (Preparation)
(separation from vivomycin)

L45 ANSWER 29 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1954:50462 HCAPLUS Full-text
DOCUMENT NUMBER: 48:50462
ORIGINAL REFERENCE NO.: 48:8966b-d
TITLE: The effect of antibiotics upon the growth of Sarcoma 180 in vivo
AUTHOR(S): Reilly, H. Christine; Stock, C. Chester; Buckley, Sonja M.; Clark, Donald A.
CORPORATE SOURCE: Sloan-Kettering Inst. for Cancer Research, New York, NY
SOURCE: Cancer Research (1953), 13, 684-7
CODEN: CNREA8; ISSN: 0008-5472
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB Actidione, actinomycin, illudin M, illudin S, and terramycin slightly retarded the growth of Crocker Sarcoma 180 in mice. With the latter 4, tumor was retarded only at doses toxic for the host. None of these compds. gave as marked effects on the development of the tumor as was previously observed with the basic protein preparation from Aspergillus fumigatus, the folic acid analogs, 6-mercaptopurine, or 2,4,6-triethylenimino-s-triazine. No tumor retardation was exhibited by aerosporin (Polymyxin B), antimycin A, aspergillic acid, Aureomycin, bacitracin, borrelidin (Na salt), candicidin, chloromycetin, circulin-HCl, citrinin, cordycepin, dihydrostreptomycin sulfate fumagillin, crude fungicidin, gliotoxin, gramicidin, neomycin, netropsin (-HCl or sulfate), phagopedin sigma (Na salt), polypeptin, rimocidin, streptomycin sulfate, streptothricin-HCl, subtilin, tyrocidine-HCl, tyrothricin, viomycin, and viscosin. Of more than 1200 crude antibiotic prepns. tested, 5 caused sufficient tumor retardation to be considered for further work.
IT 7184-60-3, Borrelidin
(effect on sarcoma growth)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-

8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

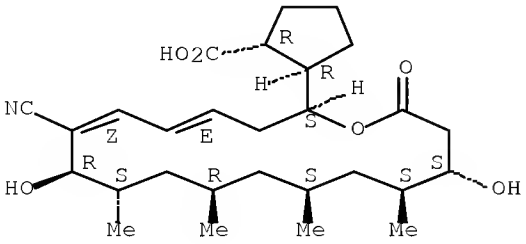
Absolute stereochemistry.
Double bond geometry as shown.



CC 11H (Biological Chemistry: Pharmacology)
IT 50-44-2, 6-Purinethiol 56-75-7, Chloramphenicol 57-62-5, Chlortetracycline 57-92-1, Streptomycin 66-81-9, Glutarimide, 3-[2-(3,5-dimethyl-2-oxocyclohexyl-2-hydroxyethyl]- 67-99-2, Gliotoxin 73-03-0, Cordycepin 79-57-2, Oxytetracycline 490-02-8, Aspergillic acid 518-75-2, Citrinin 1146-04-9, Illudin M 1149-99-1, Illudin S 1393-12-0, Rimocidin 1393-38-0, Subtilin 1397-94-0, Antimycin A 1400-61-9, Nystatin 1402-38-6, Actinomycins 1403-17-4, Candicidin 1404-04-2, Neomycin 1404-32-6, Polypeptin 1404-88-2, Tyrothricin 1405-87-4, Bacitracin 7184-60-3, Borrelidin 8011-61-8, Tyrocidine 9008-54-2, Circulin 23110-15-8, Fumagillin 27127-62-4, Viscosin 32988-50-4, Viomycin
(effect on sarcoma growth)

L45 ANSWER 30 OF 40 HCAPLUS COPYRIGHT 2008 ACS on STN
ACCESSION NUMBER: 1951:19784 HCAPLUS Full-text
DOCUMENT NUMBER: 45:19784
ORIGINAL REFERENCE NO.: 45:3505f-h
TITLE: Effect of niacin and tryptophan in counteracting toxicity of crystalline borrelidin for the rat
AUTHOR(S): Cooperman, J. M.; Rubin, S. H.; Tabenkin, B.
CORPORATE SOURCE: Hoffmann-La Roche Co., Nutley, NJ
SOURCE: Proceedings of the Society for Experimental Biology and Medicine (1951), 76, 18-20
CODEN: PSEBAA; ISSN: 0037-9727
DOCUMENT TYPE: Journal
LANGUAGE: Unavailable
AB When the crystalline antibiotic borrelidin (cf. C.A. 44, 697a) was given orally to rats, 2 γ/day had no effect on the growth rate, 10 γ/day retarded growth, and 20 γ/day resulted in a high mortality rate. The inhibition of growth by 10 γ/day was partially counteracted by supplementation with niacin. Poor growth was also obtained by adding 1-2 mg./kg. of borrelidin to the stock ration. This effect was partially overcome by feeding extra niacin or tryptophan.
IT 7184-60-3, Borrelidin
(toxicity of, effect of niacin and tryptophan on)
RN 7184-60-3 HCAPLUS
CN Cyclopentanecarboxylic acid, 2-[(2S,4E,6Z,8R,9S,11R,13S,15S,16S)-7-cyano-8,16-dihydroxy-9,11,13,15-tetramethyl-18-oxooxacyclooctadeca-4,6-dien-2-yl]-, (1R,2R)- (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.



CC 11H (Biological Chemistry: Pharmacology)
IT 7164-60-3, Borrelidin
(toxicity of, effect of niacin and tryptophan on)

L45 ANSWER 31 OF 40 MEDLINE on STN DUPLICATE 1
ACCESSION NUMBER: 2004287561 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 15186422
TITLE: Biosynthesis of the angiogenesis inhibitor borrelidin by Streptomyces parvulus Tu4055: insights into nitrile formation.
AUTHOR: Olano Carlos; Moss Steven J; Brana Alfredo F; Sheridan Rose M; Math Vidya; Weston Alison J; Mendez Carmen; Leadlay Peter F; Wilkinson Barrie; Salas Jose A
CORPORATE SOURCE: Departamento de Biologia Funcional e Instituto Universitario de Oncologia del Principado de Asturias, Universidad de Oviedo, 33006 Oviedo, Spain.
SOURCE: Molecular microbiology, (2004 Jun) Vol. 52, No. 6, pp. 1745-56.
Journal code: 8712028. ISSN: 0950-382X.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
(RESEARCH SUPPORT, NON-U.S. GOV'T)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200501
ENTRY DATE: Entered STN: 10 Jun 2004
Last Updated on STN: 2 Feb 2005
Entered Medline: 31 Jan 2005

AB The 18-membered polyketide macrolide borrelidin exhibits a number of important biological activities, including potent angiogenesis inhibition. This has prompted two recent total syntheses as well as the cloning of the biosynthetic gene cluster from Streptomyces parvulus Tu4055. Borrelidin possesses some unusual structural characteristics, including a cyclopentane carboxylic acid moiety at C17 and a nitrile moiety at C12 of the macrocyclic ring. Nitrile groups are relatively rare in nature, and little is known of their biosynthesis during secondary metabolism. The nitrile group of borrelidin is shown here to arise from the methyl group of a methylmalonyl-CoA extender unit incorporated during polyketide chain extension. Insertional inactivation of two genes in the borrelidin gene cluster, borI (coding for a cytochrome P450 monooxygenase) and borJ (coding for an aminotransferase), generated borrelidin non-producing mutants. These mutants accumulated different compounds lacking

the C12 nitrile moiety, with the product of the borI-minus mutant (12-desnitrile-12-methyl-borrelidin) possessing a methyl group and that of the borJ-minus mutant (12-desnitrile-12-carboxyl-borrelidin) a carboxyl group at C12. The former but not the latter was converted into borrelidin when biotransformed by an S. parvulus mutant that is deficient in the biosynthesis of the borrelidin starter unit. This suggests that 12-desnitrile-12-methyl-borrelidin is a competent biosynthetic intermediate, whereas the carboxylated derivative is a shunt metabolite. Bioconversion of 12-desnitrile-12-methyl-borrelidin into borrelidin was also achieved in a heterologous system co-expressing borI and borJ in Streptomyces albus J1074. This bioconversion was more efficient when borK, which is believed to encode a dehydrogenase, was simultaneously expressed with borI and borJ. On the basis of these findings, a pathway is proposed for the formation of the nitrile moiety during borrelidin biosynthesis.

CT Acyl Coenzyme A: ME, metabolism
Bacterial Proteins: GE, genetics
Bacterial Proteins: ME, metabolism
Biotransformation
Cloning, Molecular
*Fatty Alcohols: CH, chemistry
*Fatty Alcohols: ME, metabolism
Genes, Bacterial
Mixed Function Oxygenases: GE, genetics
Mixed Function Oxygenases: ME, metabolism
Mutagenesis, Insertional
Mutation
*Nitriles: CH, chemistry
*Nitriles: ME, metabolism
Oxidoreductases: GE, genetics
Oxidoreductases: ME, metabolism
Recombinant Proteins: GE, genetics
Recombinant Proteins: ME, metabolism
Streptomyces: GE, genetics
*Streptomyces: ME, metabolism
Transaminases: GE, genetics
Transaminases: ME, metabolism

RN 1264-45-5 (methylmalonyl-coenzyme A); 7184-60-3 (borrelidin)

CN 0 (Acyl Coenzyme A); 0 (Bacterial Proteins); 0 (Fatty Alcohols); 0 (Nitriles); 0 (Recombinant Proteins); EC 1.- (Mixed Function Oxygenases); EC 1.- (Oxidoreductases); EC 2.6.1.- (Transaminases)

L45 ANSWER 32 OF 40 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2004215134 MEDLINE Full-text

DOCUMENT NUMBER: PubMed ID: 15112998

TITLE: Biosynthesis of the angiogenesis inhibitor borrelidin by Streptomyces parvulus Tu4055: cluster analysis and assignment of functions.

AUTHOR: Olano Carlos; Wilkinson Barrie; Sanchez Cesar; Moss Steven J; Sheridan Rose; Math Vidya; Weston Alison J; Brana Alfredo F; Martin Christine J; Oliynyk Markiyan; Mendez Carmen; Leadlay Peter F; Salas Jose A

CORPORATE SOURCE: Departamento de Biologa Funcional e Instituto Universitario de Oncologia del Principado de Asturias, Universidad de Oviedo, 33006 Oviedo, Spain.

SOURCE: Chemistry & biology, (2004 Jan) Vol. 11, No. 1, pp. 87-97. Journal code: 9500160. ISSN: 1074-5521.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE) (RESEARCH SUPPORT, NON-U.S. GOV'T)

LANGUAGE: English

FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-AB070949; GENBANK-AF237573; GENBANK-AJ002571; GENBANK-AJ580915; GENBANK-AY045929
ENTRY MONTH: 200409
ENTRY DATE: Entered STN: 29 Apr 2004
Last Updated on STN: 1 Oct 2004
Entered Medline: 30 Sep 2004

AB The biosynthetic gene cluster for the angiogenesis inhibitor borrelidin has been cloned from Streptomyces parvulus Tu4055. Sequence analysis indicates that the macrolide ring of borrelidin is formed by a modular polyketide synthase (PKS) (borA1-A6), a result that was confirmed by disruption of borA3. The borrelidin PKS is striking because only seven rather than the nine modules expected for a nonaketide product are encoded by borA1-A6. The starter unit of the PKS has been verified as trans-cyclopentane-1,2-dicarboxylic acid (trans-1,2-CPDA), and the genes involved in its biosynthesis identified. Other genes responsible for biosynthesis of the nitrile moiety, regulation, and self-resistance were also identified.

CT *Angiogenesis Inhibitors: BI, biosynthesis
Angiogenesis Inhibitors: CH, chemistry
Cloning, Molecular
Cyclopentanes: CS, chemical synthesis
Dicarboxylic Acids: CS, chemical synthesis
Fatty Alcohols: CH, chemistry
*Fatty Alcohols: ME, metabolism
*Genes, Bacterial
Models, Chemical
Molecular Sequence Data
Molecular Structure
Multienzyme Complexes: GE, genetics
*Multigene Family
Sequence Analysis, DNA
Streptomyces: EN, enzymology
*Streptomyces: GE, genetics
Streptomyces: ME, metabolism

RN 7184-60-3 (borrelidin)

CN 0 (Angiogenesis Inhibitors); 0 (Cyclopentanes); 0 (Dicarboxylic Acids); 0 (Fatty Alcohols); 0 (Multienzyme Complexes)

L45 ANSWER 33 OF 40 BIOSIS COPYRIGHT (c) 2008 The Thomson Corporation on STN

ACCESSION NUMBER: 2006:80646 BIOSIS Full-text
DOCUMENT NUMBER: PREV200600076587
TITLE: Biosynthetic studies of the angiogenesis inhibitor borrelidin.
AUTHOR(S): Wilkinson, Barrie [Reprint Author]; Moss, Steven J.; Olano, Carlos; Brana, Alfredo F.; Sheridan, Rose M.; Weston, Alison J.; Math, Vidya; Sanchez, Cesar; Leadlay, Peter F.; Mendez, Carmen; Salas, Jose A.; Zhang, Ming Q.
CORPORATE SOURCE: Biotica Technol Ltd, Nat Prod Chem, Saffron Walden CB10 1XL, Essex, UK
barrie.wilkinson@biotica.co.uk; steven.moss@biotica.co.uk
SOURCE: Abstracts of Papers American Chemical Society, (AUG 22 2004) Vol. 228, No. Part 2, pp. U165.
Meeting Info.: Meeting of the Division of Chemical Toxicology of the American-Chemical-Society held at the 228th National Meeting of the American-Chemical-Society. Philadelphia, PA, USA. August 22 -26, 2004. Amer Chem Soc, Div Chem Toxicol.
CODEN: ACSRAL. ISSN: 0065-7727.
DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 25 Jan 2006
Last Updated on STN: 25 Jan 2006
CC General biology - Symposia, transactions and proceedings 00520
Pathology - Therapy 12512
Cardiovascular system - Physiology and biochemistry 14504
Pharmacology - General 22002
Pharmacology - Cardiovascular system 22010
Physiology and biochemistry of bacteria 31000
Food microbiology - General and miscellaneous 39008
IT Major Concepts
Pharmacology; Cardiovascular System (Transport and Circulation); Bioprocess Engineering
IT Parts, Structures, & Systems of Organisms
aorta: circulatory system
IT Chemicals & Biochemicals
borrelidin: cardiovascular-drug, biosynthesis
IT Miscellaneous Descriptors
drug synthesis
ORGN Classifier
Muridae 86375
Super Taxa
Rodentia; Mammalia; Vertebrata; Chordata; Animalia
Organism Name
rat (common)
Taxa Notes
Animals, Chordates, Mammals, Nonhuman Vertebrates, Nonhuman Mammals, Rodents, Vertebrates
ORGN Classifier
Streptomycetes and Related Genera 08840
Super Taxa
Actinomycetes and Related Organisms; Eubacteria; Bacteria; Microorganisms
Organism Name
Streptomyces parvulus (species): expression system
Taxa Notes
Bacteria, Eubacteria, Microorganisms
RN 7184-60-3 (borrelidin)

L45 ANSWER 34 OF 40 DRUGU COPYRIGHT 2008 THOMSON REUTERS on STN
ACCESSION NUMBER: 2004-36621 DRUGU C Full-text
TITLE: Stereoselective total synthesis of (-)-borrelidin.
AUTHOR: Vong B G; Kimm S H; Abraham S; Theodorakis E A
CORPORATE SOURCE: Univ.California
LOCATION: San Diego, Cal., USA
SOURCE: Angew.Chem.Int.Ed.Engl. (43, No. 30, 3947-51, 2004) 32 Ref.
CODEN: ACIEAY ISSN: 0570-0833
AVAIL. OF DOC.: Department of Chemistry and Biochemistry, University of California San Diego, 9500 Gilman Drive, MC: 0358, La Jolla, CA 92093-0358, U.S.A. (E.A.T.). (e-mail: etheodor@chem.ucsd.edu).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB A total synthesis of the antibiotic (-)-borrelidin (1) was reported. The developed synthetic route was distinguished by the construction of a strained enynone-containing macrocycle (2) and the regioselective introduction of a cyano group by implementing a novel molybdenum-catalyzed hydrostannation

reaction. Compound (1) was afforded in a yield of 88%. Spectroscopic and analytical data for (1) were in accord with reported values. The late installation of the nitrile unit in a fully functionalized macrocyclic scaffold paves the way for the preparation of analogs of (1) that could be used to evaluate structure-activity relationship data of (1).

L45 ANSWER 35 OF 40 DRUGU COPYRIGHT 2008 THOMSON REUTERS on STN
ACCESSION NUMBER: 2003-14543 DRUGU C Full-text
TITLE: Enantioselective total synthesis of borrelidin.
AUTHOR: Duffey M O; LeTiran A; Morken J P
CORPORATE SOURCE: Univ.North-Carolina
LOCATION: Chapel Hill, N.C., USA
SOURCE: J.Am.Chem.Soc. (125, No. 6, 1458-59, 2003) 1 Fig. 24 Ref.
CODEN: JACSAT ISSN: 0002-7863
AVAIL. OF DOC.: Dept. Chemistry, Venable and Kenan Labs., University of North Carolina, Chapel Hill, NC 27599-3290, U.S.A. (email: morken@unc.edu). (J.P.M.).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The enantioselective total synthesis of the angiogenesis inhibitor borrelidin (1) is described, starting with reductive aldol coupling of methyl acrylate and p-methoxybenzyloxyacetaldehyde. Iridium indanepybox-catalyzed enantioselective reductive aldol reaction established the stereogenic centers at C3, C4, C10 and C11. The method involved large scale asymmetric reductive aldol reactions and methods to reverse the usual regioselection in hydrostannylation of propargyl alcohols. The method allowed for late stage derivatization of the cyanodiene core, which may allow discovery of nontoxic analogs of the natural product.

L45 ANSWER 36 OF 40 DRUGU COPYRIGHT 2008 THOMSON REUTERS on STN
ACCESSION NUMBER: 2004-03117 DRUGU M Full-text
TITLE: In-vitro and in vivo antimalarial activities of a non-glycosidic 18-membered macrolide antibiotic, borrelidin, against drug-resistant strain of Plasmodia.
AUTHOR: Otoguro K; Ui H; Ishiyama A; Kobayashi M; Togashi H; Tokahashi Y; Masuma R; Tanaka H; Tomoda H; Omura S
CORPORATE SOURCE: Univ.Kitasato
LOCATION: Tokyo, Japan
SOURCE: J.Antibiot. (56, No. 8, 727-29, 2003) 1 Fig. 3 Tab. 14 Ref.
CODEN: JANTAJ ISSN: 0021-8820
AVAIL. OF DOC.: Kitasato Institute for Life Sciences, Kitasato University, 5-9-1 Shirokane, Minato-ku, Tokyo 108- 8642, Japan. (S.O.). (11 Authors).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB The in vivo and in vitro antimalarial activity of borrelidin (BO), isolated from the cultured broth of an actinomycete strain OM-0060, is reported. BO showed more potent in vitro activity vs. the drug-resistant K1 strain of Plasmodium falciparum than the clinically used artemether, artesunate and chloroquine and showed similar activity vs. the drug-sensitive FCR3 strain of P. falciparum to artemether and artesunate and was more potent than chloroquine. BO displayed relatively low cytotoxicity vs. MCR5 cells. BO had in vivo (s.c.) antimalarial activity vs. both rodent malaria-derived P. berghei and P. yoelii and was more effective than artemether, artesunate and

chloroquine vs. the chloroquine-resistant strain (P. yoelii). BO also showed more potent p.o. activity than artemether, artesunate and chloroquine.

L45 ANSWER 37 OF 40 DRUGU COPYRIGHT 2008 THOMSON REUTERS on STN
ACCESSION NUMBER: 2003-00062 DRUGU C Full-text
TITLE: Progress toward the total synthesis of borrelidin.
AUTHOR: Duffey M O; LeTiran A; Morken J P
CORPORATE SOURCE: Univ.North-Carolina
LOCATION: Chapel Hill, N.C., USA
SOURCE: Abstr.Pap.Am.Chem.Soc. (224 Meet., Pt. 2, ORGN 427, 2002)
CODEN: ACSRAL ISSN: 0065-7727
AVAIL. OF DOC.: Department of Chemistry, University of North Carolina, CB# 3290 Venable Hall, Chapel Hill, NC 27514, U.S.A. (e-mail: mduffey@email.unc.edu).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB A total synthesis of the antibiotic borrelidin was presented. The strategy for the synthesis of borrelidin focused on the use of an iridium-indanepybox catalyzed enantioselective reductive aldol reaction to establish the stereogenic centers at C-8, C-9, C-15, and C-16. The Authors also sought to develop a protocol for the construction of the challenging acrylonitrile moiety at C-7. In order to accomplish these goals a retrosynthetic approach involving the synthesis of two main fragments, alkyne (1) and vinyl iodide (2), to produce the core structure of borrelidin, was envisioned. The synthesis of (1-2) was reported. (conference abstract: 224th ACS National Meeting, Boston, Massachusetts, USA, 2002).

L45 ANSWER 38 OF 40 DRUGU COPYRIGHT 2008 THOMSON REUTERS on STN
ACCESSION NUMBER: 2001-09193 DRUGU B P Full-text
TITLE: Borrelidin inhibits a cyclin-dependent kinase (CDK), Cdc28/Cln2, of Saccharomyces cerevisiae.
AUTHOR: Tsuchiya E; Yukawa M; Miyakawa T; Kimura K I; Takahashi H
CORPORATE SOURCE: Univ.Hiroshima; Snow-Brand-Milk-Products
LOCATION: Hiroshima; Tochigi, Jap.
SOURCE: J.Antibiot. (54, No. 1, 84-90, 2001) 5 Fig. 21 Ref.
CODEN: JANTAJ ISSN: 0021-8820
AVAIL. OF DOC.: Department of Molecular Biotechnology, Graduate School of Advanced Sciences of Matter, Hiroshima University, Higashi-Hisroshima 739-8527, Japan. (e-mail: stsuchi@hiroshima-u.ac.jp).
LANGUAGE: English
DOCUMENT TYPE: Journal
FIELD AVAIL.: AB; LA; CT
FILE SEGMENT: Literature
AB Borrelidin was identified as an inhibitor of cyclin-dependent kinase (CDK) of the budding yeast Sacch. cerevisiae Cdc28/Cln2. Borrelidin was shown to arrest both haploid and diploid cells in G1 phase at the point indistinguishable from that of alpha-mating pheromone, at concentrations that did not afect the gross protein synthesis. Results suggest that borrelidin may be a useful lead in the development of new CDK inhibitors of higher eukaryotes.

L45 ANSWER 39 OF 40 DRUGU COPYRIGHT 2008 THOMSON REUTERS on STN
ACCESSION NUMBER: 3199 DRUGU
FILE SEGMENT: Registry

DERWENT DRUG REGISTRY NAME: BORRELIDI
DERWENT DRUG NAME: BORRELIDIN
CAS REGISTRY NUMBER: 7184-60-3
CONTROLLED TERM: ANTIBIOTICS
SUBSTRUCTURE TERM: MACROCYCLE; CYCLOPENTANE; LACTONE; POLYOLEFIN; POLYALCOHOL HYDROXYACID; NITRILE; OXACYCLOOCTADECANE; AH-LINKED-CC
MULTIPUNCH CODE: 02& *G; 02- *G; 04& *G; 047 *G; 06& *G; 068 *G; 075 *G; 078 *G; 091 *G; 094 *G; 10- *G; 103 *G; 105 *G; 106 *G; 108 *G; 109 *G; 12& *G; 12- *G; 13& *G; 134 *G; 164 *G; 17- *G; 176 *G; 18- *G; 182 *G; 232 *G; 237 *G; 254 *G; 257 *G

L45 ANSWER 40 OF 40 EMBASE COPYRIGHT (c) 2008 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 1974191119 EMBASE Full-text
TITLE: Alteration of structure or level of threonyl tRNA synthetase in borrelidin resistant mutants of E. coli.
AUTHOR: Nass, G.; Thomale, J.
CORPORATE SOURCE: Abt. Molek. Biol., Max Planck Inst. Exp. Med., Gottingen, Germany.
SOURCE: FEBS Letters, (1974) Vol. 39, No. 2, pp. 182-186.
ISSN: 0014-5793 CODEN: FEBLAL
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology: Bacteriology, Mycology, Parasitology and Virology
029 Clinical and Experimental Biochemistry
LANGUAGE: English

AB Borrelidin inhibits the growth of E. coli effectively. Since no other biochemical reaction is known to be attacked directly by Borrelidin than the enzymatic activity of the threonyl-t RNA synthetase (ThRS), Borrelidin resistant mutants of E. coli K12 and E. coli B were isolated with the aim of finding mutants with an altered structure or level of ThRS. The ThRS of 15 Borrelidin resistant mutants of each E. coli strain was investigated. The characterization of the ThRS of some Borrelidin resistant mutants is described. By means of determination of enzyme constants and antibody neutralization curves it is shown that the Borrelidin resistant mutants can be divided into 3 groups: one group of mutants exhibits constitutively increased levels of wildtype ThRS, the second group structurally altered ThRS, and in a third group of mutants no alteration of the structure or level of ThRS could be detected. This suggests that Borrelidin resistance in the latter mutants is due to some other reason than alteration of ThRS activity. Since it is known that the ThRS participates in the regulation of formation of the threonine biosynthetic enzymes, the level of aspartokinase was also determined in the Borrelidin resistant mutants grown in the presence and absence of Borrelidin.

CT Medical Descriptors:
*escherichia coli
in vitro study
microorganism
*mutant
theoretical study
CT Drug Descriptors:
*borrelidin
*threonine transfer rna ligase
RN (borrelidin) 7184-60-3; (threonine transfer RNA ligase) 9023-46-5

***** SEARCH HISTORY *****

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     FILE 'HCAPLUS' ENTERED AT 08:15:16 ON 04 SEP 2008
L1             1 SEA ABB=ON  PLU=ON  US20070065920/PN
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L2               SCR 2043 OR 1918
L3               STRUCTURE UPLOADED
                 D

Uploading L11.str
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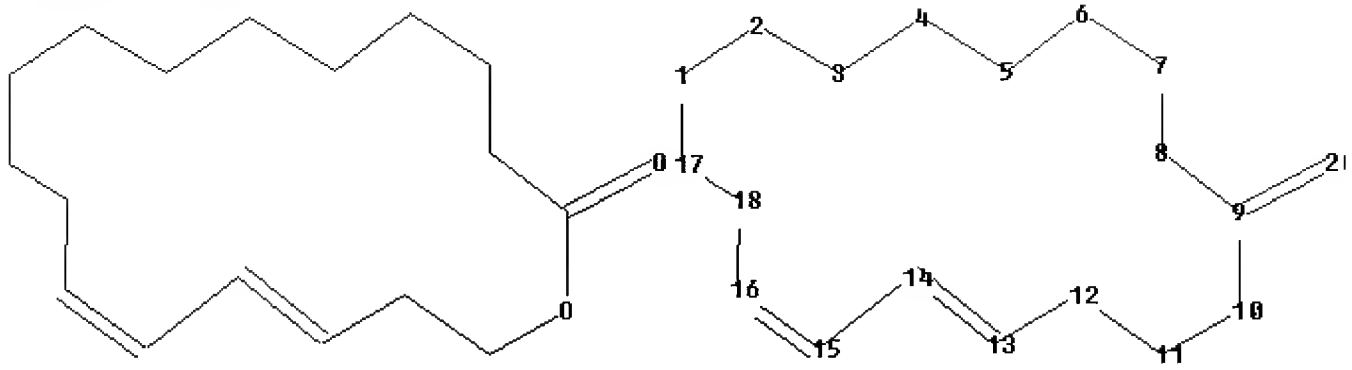


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ring nodes :
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chain bonds :
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ring bonds :
1-2  1-17  2-3  3-4  4-5  5-6  6-7  7-8  8-9  9-10  10-11  11-12  12-13  13-14  14-
15
15-16  16-18  17-18
exact/norm bonds :
9-20
exact bonds :
1-2  1-17  2-3  3-4  4-5  5-6  6-7  7-8  8-9  9-10  10-11  11-12  12-13  13-14  14-
15
15-16  16-18  17-18
isolated ring systems :
containing 1 :


Match level :
1:Atom  2:Atom  3:Atom  4:Atom  5:Atom  6:Atom  7:Atom  8:Atom  9:Atom  10:Atom
11:Atom  12:Atom  13:Atom  14:Atom  15:Atom  16:Atom  17:Atom  18:Atom  20:CLASS




L4             2 SEA SSS SAM L3 NOT L2
L5            68 SEA SSS FUL L3 NOT L2
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L6               STRUCTURE UPLOADED
                 D
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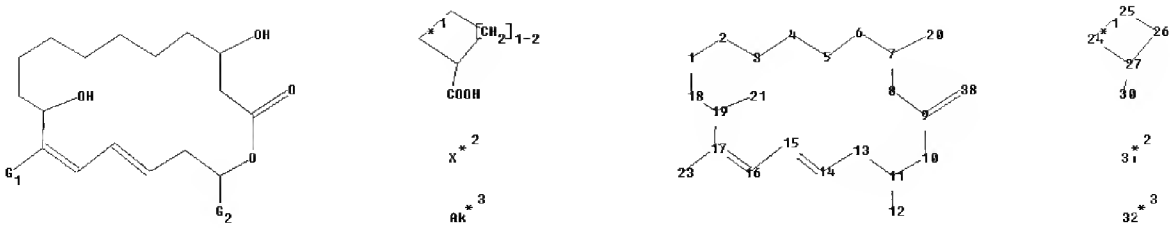
Uploading L12.str



chain nodes :
12 20 21 23 30 31 32 38
ring nodes :
1 2 3 4 5 6 7 8 9 10 11 13 14 15 16 17 18 19 24 25 26 27
chain bonds :
7-20 9-38 11-12 17-23 19-21 27-30
ring bonds :
1-2 1-18 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-13 13-14 14-15 15-16
16-17 17-19 18-19 24-25 24-27 25-26 26-27
exact/norm bonds :
7-20 9-38 11-12 17-23 19-21
exact bonds :
1-2 1-18 2-3 3-4 4-5 5-6 6-7 7-8 8-9 9-10 10-11 11-13 13-14 14-15 15-16
16-17 17-19 18-19 24-25 24-27 25-26 26-27 27-30
isolated ring systems :
containing 1 : 24 :

G1:CH3,COOH,CN

G2:[*1],[*2],[*3]

Match level :
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:Atom 8:Atom 9:Atom 10:Atom
11:Atom 12:CLASS 13:Atom 14:Atom 15:Atom 16:Atom 17:Atom 18:Atom 19:Atom
20:CLASS 21:CLASS
23:CLASS 24:Atom 25:Atom 26:Atom 27:Atom 30:CLASS 31:CLASS 32:CLASS
38:CLASS

L7 0 SEA SUB=L5 SSS SAM L6

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L8 86 SEA ABB=ON PLU=ON L5

FILE 'REGISTRY' ENTERED AT 08:44:27 ON 04 SEP 2008
L9 17 SEA SUB=L5 SSS FUL L6

FILE 'HCAPLUS' ENTERED AT 08:44:57 ON 04 SEP 2008
L10 86 SEA ABB=ON PLU=ON L9

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L12         5382 SEA ABB=ON  PLU=ON  BIOSYNTHE? GENE#
L13            4 SEA ABB=ON  PLU=ON  L10 AND L12
L14         5465 SEA ABB=ON  PLU=ON  POLYKETID?
L15            6 SEA ABB=ON  PLU=ON  L10 AND L14
L16           18 SEA ABB=ON  PLU=ON  L11 OR L13 OR L15
L17           19 SEA ABB=ON  PLU=ON  L10 AND PHARMAC?/SC,SX
L18           33 SEA ABB=ON  PLU=ON  L16 OR L17
L19        36472 SEA ABB=ON  PLU=ON  BIOSYNTHET?
L20            9 SEA ABB=ON  PLU=ON  L10 AND L19
L21           37 SEA ABB=ON  PLU=ON  L18 OR L20
L22          478 SEA ABB=ON  PLU=ON  SALAS J?/AU
L23          305 SEA ABB=ON  PLU=ON  MENDEZ C?/AU
L24           51 SEA ABB=ON  PLU=ON  OLANO C?/AU
L25         3325 SEA ABB=ON  PLU=ON  SANCHEZ C?/AU
L26          100 SEA ABB=ON  PLU=ON  BRANA A?/AU
L27          449 SEA ABB=ON  PLU=ON  WILKINSON B?/AU
L28         5002 SEA ABB=ON  PLU=ON  MARTIN C?/AU
L29         1074 SEA ABB=ON  PLU=ON  MOSS S?/AU
L30          197 SEA ABB=ON  PLU=ON  LEADLAY P?/AU
L31           16 SEA ABB=ON  PLU=ON  OLIYNYK M?/AU

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L32            1 SEA ABB=ON  PLU=ON  L9 AND (MEDLINE OR BIOSIS OR DRUGU OR
                 EMBASE)/LC

     FILE 'MEDLINE' ENTERED AT 08:57:41 ON 04 SEP 2008
L33           31 SEA ABB=ON  PLU=ON  L32
L34            3 SEA ABB=ON  PLU=ON  L33 AND BIOSYNTHET?
                 D TI KWIC 1-3

     FILE 'BIOSIS' ENTERED AT 08:58:27 ON 04 SEP 2008
L35           63 SEA ABB=ON  PLU=ON  L32
L36            6 SEA ABB=ON  PLU=ON  L33 AND BIOSYNTHET?

     FILE 'DRUGU' ENTERED AT 08:58:53 ON 04 SEP 2008
L37            0 SEA ABB=ON  PLU=ON  L33 AND BIOSYNTHET?
L38            8 SEA ABB=ON  PLU=ON  L32
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                 D TI KWIC 1-4

     FILE 'EMBASE' ENTERED AT 08:59:36 ON 04 SEP 2008
L39            3 SEA ABB=ON  PLU=ON  L33 AND BIOSYNTHET?

     FILE 'MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 09:00:06 ON 04 SEP 2008

L40          176 SEA ABB=ON  PLU=ON  ((L22 OR L23 OR L24 OR L25 OR L26 OR L27
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L41            6 SEA ABB=ON  PLU=ON  L40 AND BORRELIDIN
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     FILE 'HCAPLUS' ENTERED AT 09:04:34 ON 04 SEP 2008
L42            7 SEA ABB=ON  PLU=ON  (((L22 OR L23 OR L24 OR L25 OR L26 OR L27
                 OR L28 OR L29 OR L30 OR L31)) AND L10) OR (L1 AND L10)
L43           30 SEA ABB=ON  PLU=ON  L21 NOT L42
                 SAVE TEMP L42 KAM240HCAIN/A
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                SAVE TEMP L43 KAM240HCAP/A

     FILE 'STNGUIDE' ENTERED AT 09:06:18 ON 04 SEP 2008
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                D QUE L41

     FILE 'HCAPLUS, MEDLINE, BIOSIS, EMBASE' ENTERED AT 09:10:22 ON 04 SEP 2008
L44           8 DUP REM L42 L41 (5 DUPLICATES REMOVED)
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                      ANSWER '8' FROM FILE BIOSIS
                D L44 1-7 IBIB ABS HITSTR
                D L44 8 IBIB AB
                D QUE L43
                D QUE L34
                D QUE L36
                D QUE L38
                D QUE L39

     FILE 'HCAPLUS, MEDLINE, BIOSIS, DRUGU, EMBASE' ENTERED AT 09:11:54 ON 04
     SEP 2008
L45          40 DUP REM L43 L34 L36 L38 L39 (10 DUPLICATES REMOVED)
                      ANSWERS '1-30' FROM FILE HCAPLUS
                      ANSWERS '31-32' FROM FILE MEDLINE
                      ANSWER '33' FROM FILE BIOSIS
                      ANSWERS '34-39' FROM FILE DRUGU
                      ANSWER '40' FROM FILE EMBASE
                D L45 1-30 IBIB ABS FHITSTR HITIND
                D L45 31-40 IBIB AB HITIND
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